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Research Paper

Relevance of DNA repair gene polymorphisms to gastric cancer risk and phenotype

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ABSTRACT

Variations in DNA repair genes have been reported as key factors in gastric cancer (GC) susceptibility but results among studies are inconsistent. We aimed to assess the relevance of DNA repair gene polymorphisms and environmental factors to GC risk and phenotype in a Caucasian population in Spain. Genomic DNA from 603 patients with primary GC and 603 healthy controls was typed for 123 single nucleotide polymorphisms in DNA repair genes using the Illumina platform. *Helicobacter pylori* infection with CagA strains (odds ratio (OR): 1.99; 95% confidence interval (CI):

1.55–2.54), tobacco smoking (OR: 1.77; 95% CI: 1.22–2.57), and family history of GC (OR: 2.87; 95% CI: 1.85–4.45) were identified as independent risk factors for GC. By contrast, the *TP53* rs9894946A (OR: 0.73; 95% CI: 0.56–0.96), *TP53* rs1042522C (OR: 0.76; 95% CI: 0.56–0.96), and *BRIP1* rs4986764T (OR: 0.55; 95% CI: 0.38–0.78) variants were associated with lower GC risk. Significant associations with specific anatomopathological GC subtypes were also observed, most notably in the *ERCC4* gene with the rs1799801C, rs2238463G, and rs3136038T variants being inversely associated with cardia GC risk. Moreover, the *XRCC3* rs861528 allele A was significantly increased in the patient subgroup with diffuse GC (OR: 1.75; 95% CI: 1.30–2.37). Our data show that specific *TP53*, *BRIP1*, *ERCC4*, and *XRCC3* polymorphisms are relevant in susceptibility to GC risk and specific subtypes in Caucasians.

INTRODUCTION

Gastric cancer (GC) represents the fifth most common neoplasia and the third leading cause of cancer–related death worldwide [1]. Despite continuous advances in diagnosis and treatment, most patients with GC present with late–stage disease and poor prognosis. Therefore, it is not surprising that detection of potential risk factors is regarded as the most effective option to prevent and reduce the incidence of GC.

GC is a heterogeneous disease that shows distinct clinical, epidemiological, and molecular features among tumors arising from the proximal (cardia) or distal (non–cardia) stomach, and among intestinal and diffuse histological subtypes [2, 3]. These differences in phenotype seem to be determined by complex interactions between environmental and host genetic factors. Among them, *Helicobacter pylori* (*H. pylori*) infection has been identified as the single most common cause of GC [4]. This organism, which colonizes over half of the world's population, first induces a chronic superficial gastritis in virtually all infected people, initiating a process that in certain individuals may lead to GC [5]. Several studies have found that bacterial virulence determinants, such as the presence of the CagA pathogenicity island, are associated with a higher risk of GC development [6, 7]. However, why only a minority (< 1%) of infected individuals develops gastric malignancy remains a matter of speculation, suggesting that factors other than bacterial infection alone are involved in the carcinogenesis process.

Additional host genetic factors are also likely to contribute in gastric carcinogenesis. In this respect, genetic susceptibility may be critical in several relevant processes such as mucosal protection, immune response, carcinogen detoxification, antioxidant protection, cell proliferation, and DNA repair [8]. Concerning the latter, a complex system involving multiple enzymes and pathways plays a crucial role in maintaining genome homeostasis in the face of exogenous and endogenous agents and general DNA replication errors. In this context, five major DNA repair pathways have been described: i) base excision repair (BER) fixes simple base modifications (oxidized/reduced bases) and DNA single-strand breaks caused by ionizing radiation, alkylating agents, and oxidative stress [9]; ii) nucleotide excision repair (NER) repairs the damage caused by bulky adducts produced by ultraviolet light and a wide array of chemical agents [10]; iii) mismatch repair (MMR) removes base–base mismatches, small loops, and insertion/deletion mispairs occurring during DNA replication and recombination [11]; iv) double–strand break repair (DSBR) evolves two main mechanisms, non–homologous end joining and homologous recombination repair, whichrepair the most severe type of DNA damage [12] and v) direct reversion repair (DR) corrects methylated bases, namely O^6-methylguanine (O^6MeG), induced by alkylating agents [13].

DNA repair genes harbor functional polymorphic regions that have been reported to influence the host capacity to repair damaged DNA. Therefore, it is plausible that individuals carrying deficient DNA repair alleles will be at greater risk of presenting mutations that can alter genome integrity and stability leading to cancer development. Common single nucleotide polymorphisms (SNPs) in DNA repair genes have been identified as potential risk factors for a wide array of cancers, including lung [14], ovarian [15], prostate [16], and breast cancer [17]. However, the data are not conclusive concerning the relationship between DNA repair variants and GC; whereas some studies report a link with GC risk [18, 19] or anatomopathological subtypes [20, 21], other studies have failed to confirm any associations [22, 23].

Trying to address this issue, we sought to evaluate the influence of 123 selected DNA repair gene polymorphisms and environmental factors (*H. pylori* infection and smoking habits) to GC risk and phenotype in a Caucasian population in Spain. Because GC shows marked heterogeneity in histology and anatomic involvement, we aimed also to analyze the role of both environmental and host genetic factors with regard to the site and histological type of the tumor.

RESULTS

Clinical and demographic characteristics of GC patients and healthy controls

The clinical and demographic characteristics of GC patients and healthy controls (HCs) are shown in

Table 1. Of the 603 patients with GC, 117 (19.4%) were classified as cardia and 486 (80.6%) as non–cardia GC cases. According to Lauren's classification [3], non–cardia gastric adenocarcinomas were of intestinal histotype in 250 patients (51.4%), diffuse histotype in 178 patients (36.6%), and mixed or undetermined type in 58 patients (11.9%). Among the evaluated features, infection with *H. pylori* and *CagA*+ strains was significantly associated with a higher risk of GC (*H. pylori*, odds ratio (OR): 1.38; 95% confidence interval (CI): 1.09–1.76; $P = 0.008$; *CagA*+ strains, OR: 1.95; 95% CI: 1.54–2.46; $P < 0.0001$). However, no differences in the prevalence of *VacA*+ strains were observed between GC patients and controls (40.1% *vs.* 39.3%). When considering the anatomic location of the tumor, infection with *CagA*+ strains was specifically associated with a higher risk of developing non–cardia GC (62.6% *vs*. 41.3%; OR: 2.32; 95% CI: 1.80–2.98; $P < 0.0001$) (Supplementary Table 1). Of interest, no association between *H. pylori* infection and cardia GC was found. Among non–cardia GC patients, *H. pylori* infection with *CagA*+ strains was significantly more frequent in both diffuse and intestinal tumor subtypes compared with controls (OR: 3.02; 95% CI: 2.08–4.37; $P < 0.0001$ *vs.* HC; and OR: 2.25; 95% CI: 1.65–3.07; $P < 0.0001$ *vs*. HC, respectively).

In addition to *H. pylori* infection, active smoking (OR: 1.53; 95% CI: 1.12–2.09) and family history of GC (OR: 3.02; 95%: 1.99–4.60) were also found to be risk factors for the development of GC (Table 1). Stratified analysis by tumor location showed that smoking habit was strongly associated with cardia GC (OR: 2.93; 95% CI: 1.68–5.11; $P = 0.0002$) whereas a positive family history of GC was specifically associated with a higher risk of non–cardia GC (OR: 3.29; 95% CI: 2.14–5.06; $P < 0.0001$), (Supplementary Table 1).

Genotyping

Single marker analysis

Of the 123 SNPs initially evaluated in our study, 108 SNPs were successfully genotyped in 1206 subjects (603 GC patients and 603 HCs) and available for analysis. Supplementary Table 2 summarizes the genotype distribution of each polymorphism in GC patients and controls according to the location and histological type of the tumor. Genotype frequencies did not deviate significantly from those expected under Hardy–Weinberg equilibrium in the control group. Moreover, no evidence of genetic heterogeneity among study participants, either patients or controls, was observed (data not shown).

Fourteen SNPs (*TP53* rs1042522, *RAD52* rs11226, *ERCC5* rs17655, *POLG* rs176641, *BRCA2* rs1801406, *LIG3* rs2074522, *XPC* rs2228000, *ERCC4* rs2238463, *MGMT* rs2308321, *MSH3* rs26779, *ERCC4* rs3136038, *BRIP1* rs4986764, *XRCC3* rs861528, and *TP53* rs9894946) revealed significant associations with GC risk ($P < 0.05$) in at least one of the four genetic models evaluated in the analysis (Supplementary Table 3). However, after false discovery rate (FDR) multiple test correction, only four SNPs in the *TP53* (rs1042522G>C, rs9894946G>A), *LIG3* (rs2074522G>A), and *BRIP1* (rs4986764C>T) genes retained significance (Table 2). Thus, the *TP53* rs1042522C and *TP53* rs9894946A variants were inversely associated with GC risk (dominant models, OR: 0.67; 95% CI: 0.53–0.85; and OR: 0.69; 95% CI: 0.53–0.90, respectively). The *BRIP1* rs4986764T variant also showed a protective effect (recessive model, OR: 0.59; 95% CI: 0.42–0.83). By contrast, the rare allele A of *LIG3* rs2074522 was associated with a higher risk of developing the disease (recessive model, OR: 0.59; 95% CI: 1.58–31.5).

None of the 108 DNA repair gene polymorphisms analyzed in our study were significantly associated with prevalence of infection with *H. pylori* or CagA/VacA strains (Supplementary Table 4). Of note, when subgroup analysis by *H. pylori* infection status was performed, the previously reported risk associations of *TP53* rs1042522, *TP53* rs9894946G, *LIG3* rs2074522, and *BRIP1* rs4986764 with GC were observed only in the group of *H. pylori*–infected individuals (Table 2). However, after FDR corrections, these associations did not remain significant with the exception of *TP53* rs1042522 (P72R). Tests for interaction under a multiplicative model showed no statistically significant interactions between *TP53* rs1042522 genotypes and *H. pylori* infection ($P\text{-}_{interaction} = 0.081$, dominant model).

On the other hand, stratified analysis by tumor location (cardia/distal) and histological type of GC (intestinal/diffuse) showed significant associations with specific GC subtypes (Supplementary Tables 5 and 6). Table 3 summarizes those SNPs significantly associated with GC subtypes after applying the FDR correction test. Of interest, three SNPs (rs1799801, rs2238463, and rs3136038) located in the NER gene *ERCC4* were inversely associated with cardia GC risk. The *ERCC4* rs2238463 and rs3136038 loci were in strong linkage disequilibrium (LD) in our data set ($D' = 1$, $r^2 = 0.92$) with lower values for the rs1799801/rs2238463 ($D' = 0.98$, $r^2 = 0.70$), and rs1799801/rs3136038 ($D' = 0.93$, $r^2 = 0.69$) loci. In addition, carriers of the *XRCC3* rs861528A and *POLG* rs176641C variants were significantly increased in the subgroup of patients with non–cardia GC compared to controls (dominant models, OR: 1.45; 95% CI: 1.11–1.88; and OR: 1.40, 95% CI: 1.09–1.81, respectively). By contrast, the *XPC* rs2228000T variant was associated with a lower risk of non–cardia GC (dominant model, OR: 0.70; 95% CI: 0.55–0.90). When considering the histological type of tumor, the most remarkable association was observed in the DSBR gene *XRCC3*, with the A allele of rs861528 being associated with a higher risk of diffuse GC (dominant model, OR: 2.11; 95% CI: 1.43–3.12) (Table 3.).

Table 1: Demographic and clinical characteristics of healthy controls and gastric cancer patients

	Healthy Controls *n* = 603	GC patients *n* = 603	ORs (95% CI)	*P* Value
Age yrs ± SD (range)	70.17 ± 12.32 (30–96)	70.32 ± 12.27 (29–96)		0.97
Gender	413 M (68.5%) 190 F (31.5%)	413 M (68.5%) 190 F (31.5%)	1 (0.78–1.27)	1.04
[a]Cigarette smoking				
Never	311/585 (53.2%)	291/582 (50%)	Reference	
Former	184/585 (31.4%)	162/582 (27.8 %)	0.94 (0.72–1.23)	0.68
Current smoker	90/585 (15.4%)	129/582 (22.2%)	1.53 (1.12–2.09)	0.009
[b]*H. pylori* +	364 (60.4%)	377/556 (67.8%)	1.38 (1.09–1.76)	0.008
CagA+	253 (41.9%)	325/556 (58.4%)	1.95 (1.54–2.46)	< 0.0001
VacA+	237 (39.3%)	223/556 (40.1%)	1.03 (0.82–1.31)	0.81
[c]Family history of GC	33/539 (6.1%)	88/534 (16.5%)	3.02 (1.99–4.60)	< 0.0001
Neoplasia location				
Cardia		117 (19.4%)		
Non–cardia		486 (80.6%)		
Lauren's classification				
Intestinal		250 (51.4%)		
Diffuse		178 (36.6%)		
Mixed or undetermined		58 (11.9%)		
[d]TNM stage				
Stage I		80 (13.3%)		
Stage II		79 (13.1%)		
Stage III		131 (21.7%)		
Stage IV		264 (43.8%)		
Could not be assessed		49 (8.1%)		
Surgical treatment		410 (68%)		
Chemotherapy		225 (37.3%)		
Radiotherapy		105 (17.4%)		

GC, gastric cancer; n, number of individuals; OR, odds ratio; CI, confidence interval; SD, standard deviation; M, male; F, female.
[a]Information was available for 585 HC and 582 GC patients.
[b]*Helicobacter pylori* infection and CagA/VacA antibody data obtained by western blot analysis in serum samples. Information was available for 603 HC and 556 GC patients.
[c]Information was available for 539 HC and 534 GC patients.
[d]Clinical tumor stages according to the International Union Against Cancer (UICC) criteria. In 49 GC patients tumor stage could not be assessed.

Finally, no significant differences in genotype distribution and allele frequencies between GC patients and controls were found when subjects were stratified according to other evaluated features such as age, gender, smoking habit, and family history of GC (Supplementary Tables 7–10).

Haplotype analysis

The comparisons of common haplotype frequencies (> 0.05) in each gene block between GC patients and controls are presented in Supplementary Table 11. Haplotype analysis revealed significant differences in four blocks covering the *BRIP1*, *ERCC4*, *ERCC5*, and *TP53* genes (Table 4, Figure 1). The most robust association was observed in the *TP53* block. Thus, the haplotype rs1042522C, rs1614984C, and rs9894946A, at a frequency of 10% in our population, was inversely associated with GC risk (12% in HC *vs.* 8% in GC; OR: 0.68; 95% CI: 0.51–0.91). This haplotype contains the rs1042522C and rs9894946A alleles previously reported in the single SNP analysis as protective factors

Table 2: Association of DNA repair gene polymorphisms with GC risk

Gen	db SNP ID	A/a	*H. pylori*	HC Genotype			GC Genotype			Dominant model			Recessive model			Log-Additive model		
				AA	Aa	aa	AA	Aa	aa	OR (95% CI)[a]	*P*-value	FDR[b]	OR (95% CI)[a]	*P*-value	FDR[b]	OR (95% CI)[a] *P*-value		FDR[b]
TP53	rs1042522	G/C	Overall n	314	247	40	372	192	39	0.67 (0.53–0.85)	**0.001**	**0.012**	1.05 (0.66–1.67)	0.832	0.896	0.78 (0.65–0.94)	**0.009**	0.068
			H. pylori +	180	159	23	241	115	21	0.55 (0.41–0.74)	**0.0001**	**0.002**	0.85 (0.46–1.58)	0.619	0.734	0.65 (0.51–0.83)	**0.001**	**0.013**
			H. pylori –	134	88	17	103	59	17	0.95 (0.64–1.41)	0.803	0.902	1.35 (0.66–2.74)	0.413	0.912	1.02 (0.76–1.39)	0.875	0.983
TP53	rs9894946	G/A	Overall n	409	165	18	452	138	6	0.69 (0.53–0.90)	**0.006**	**0.013**	0.23 (0.08–0.68)	**0.002**	**0.014**	0.66 (0.52–0.85)	**0.001**	**0.017**
			H. pylori +	249	98	11	288	82	3	0.65 (0.46–0.91)	**0.019**	0.095	0.27 (0.07–0.97)	**0.021**	0.143	0.64 (0.47–0.87)	**0.004**	0.053
			H. pylori –	160	67	7	132	44	1	0.73 (0.47–1.14)	0.168	0.832	0.19 (0.02–1.57)	0.065	0.674	0.70 (0.47–1.05)	0.085	0.659
LIG3	rs2074522	G/A	Overall n	509	89	2	496	94	13	1.22 (0.89–1.67)	0.217	0.268	7.05 (1.58–31.5)	**0.001**	**0.014**	1.32 (0.99–1.75)	0.055	0.080
			H. pylori +	306	54	2	309	59	9	1.23 (0.83–1.81)	0.302	0.393	4.3 (0.92–20.28)	**0.035**	0.143	1.30 (0.92–1.85)	0.135	0.201
			H. pylori –	203	35	–	148	27	4	1.16 (0.68–1.97)	0.591	0.902	NA		NA	1.33 (0.80–2.11)	0.296	0.659
BRIP	rs4986764	C/T	Overall n	224	270	107	232	297	69	0.94 (0.74–1.20)	0.633	0.724	0.59 (0.42–0.83)	**0.002**	**0.015**	0.85 (0.72–1.00)	0.055	0.075
			H. pylori +	134	166	64	145	188	42	0.93 (0.69–1.26)	0.657	0.603	0.58 (0.38–0.89)	**0.011**	0.143	0.84 (0.68–1.04)	0.106	0.180
			H. pylori –	90	104	43	68	89	21	0.99 (0.66–1.48)	0.866	0.908	0.62 (0.35–1.09)	0.089	0.686	0.87 (0.66–1.16)	0.451	0.836

Stratified analysis by *H. pylori* infection status.
HC, healthy control; GC, gastric cancer; n, number of individuals.
A/a, major/minor alleles; OR, odds ratio; CI, confidence interval; NA, not applied.
[a]*P*-values, ORs, and 95% CIs adjusted by gender, age, smoking habit, and family history of GC.
[b]Q_{FDR}-values obtained after applying the False Discovery Rate (FDR) test.
P-values < 0.05 are highlighted in bold.

for the development of GC. In the same way, the *BRIP1* (rs2048718T, rs4968451C, rs4986764T) and *ERCC4* (rs1799801T, rs1800067G, rs2238463G, rs3136038T) haplotypes carry the risk alleles identified in the single SNP–based analysis, associated with overall GC risk and cardial subtype, respectively. Stratified haplotype analysis by tumor location and GC histological type did not provide additional information beyond individual SNP results (data not shown).

Multivariate analysis

In summary, of the environmental and genetic factors evaluated in this study, logistic regression analysis

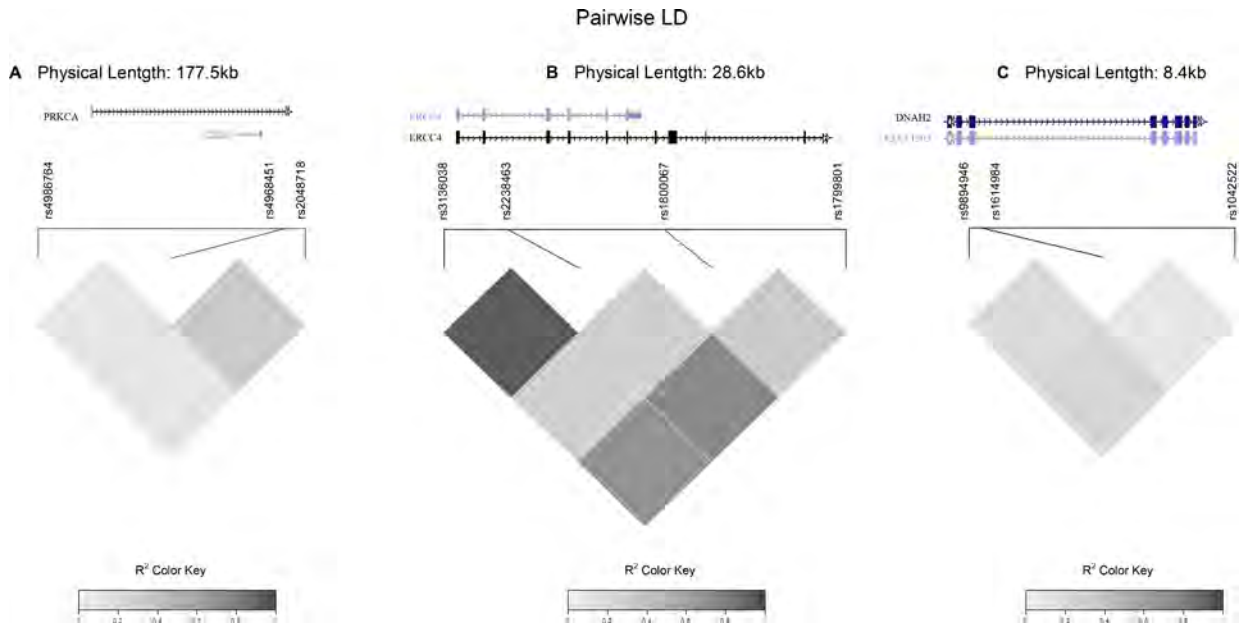

Figure 1: Linkage disequilibrium (LD) maps covering the *BRIP1*, *ERCC4*, and *TP53* genes. LD maps based on pairwise r^2 values for SNPs investigated in the (**A**) *BRIP1* gene, (**B**) *ERCC4* gene, and (**C**) *TP53* gene. Gene annotations obtained from the UCSC genome browser. Only LD maps of haplotypes in DNA repair genes significantly associated with gastric cancer risk ($P < 0.05$) are shown in the figure.

Table 3: Association of DNA repair gene polymorphisms with anatomical and histological subtypes of gastric cancer

CARDIA GC			HC Genotype			GC Genotype			Dominant model		Recessive model		Log-Additive model	
Gen	db SNP ID	A/a	AA	Aa	aa	AA	Aa	aa	OR (95% CI)[a]	FDR[b]	OR (95% CI)[a]	FDR[b]	OR (95% CI)[a]	FDR[b]
ERCC4	rs1799801	T/C	280	261	59	71	35	11	0.58 (0.38-0.88)	**0.036**	0.84 (0.40-1.77)	0.640	0.69 (0.49-0.97)	0.077
ERCC4	rs2238463	C/G	210	303	89	58	44	15	0.54 (0.35-0.81)	**0.036**	0.79 (0.42-1.49)	0.555	0.67 (0.49-0.92)	0.077
ERCC4	rs3136038	C/T	222	298	81	58	44	14	0.57 (0.38-0.87)	**0.036**	0.80 (0.42-1.53)	0.555	0.69 (0.50-0.96)	0.077
NON-CARDIA GC			**HC Genotype**			**GC Genotype**			**Dominant model**		**Recessive model**		**Log-Additive model**	
Gen	**db SNP ID**	**A/a**	**AA**	**Aa**	**aa**	**AA**	**Aa**	**aa**	**OR (95% CI)[a]**	**FDR[b]**	**OR (95% CI)[a]**	**FDR[b]**	**OR (95% CI)[a]**	**FDR[b]**
XPC	rs2228000	C/T	267	277	59	255	187	44	0.70 (0.55-0.90)	**0.034**	0.98 (0.64-1.48)	0.907	0.81 (0.67-0.98)	0.067
XRCC3	rs861528	G/A	350	205	33	218	176	27	1.45 (1.11-1.88)	**0.034**	1.21 (0.71-2.06)	0.626	1.31 (1.06-1.62)	0.067
POLG	rs176641	A/C	262	266	75	170	253	62	1.40 (1.09-1.81)	**0.041**	1.04 (0.72-1.50)	0.895	1.21 (1.00-1.46)	0.071
TP53	rs1042522	G/C	314	247	40	302	149	35	0.67 (0.52-0.87)	**0.028**	1.03 (0.76-1.97)	0.582	0.80 (0.65-0.98)	0.067
LIG3	rs2074522	G/A	509	89	2	393	81	12	1.37 (0.99-1.90)	0.084	7.94 (1.7-35.91)	**0.027**	1.46 (1.09-1.96)	0.067
BRIP1	rs4986764	C/T	224	270	107	197	230	56	0.87 (0.67-1.11)	0.315	0.59 (0.41-0.85)	**0.037**	0.81 (0.68- 0.97)	0.067
INTESTINAL GC			**HC Genotype**			**GC Genotype**			**Dominant model**		**Recessive model**		**Log-Additive model**	
Gen	**db SNP ID**	**A/a**	**AA**	**Aa**	**aa**	**AA**	**Aa**	**aa**	**OR (95% CI)[a]**	**FDR[b]**	**OR (95% CI)[a]**	**FDR[b]**	**OR (95% CI)[a]**	**FDR[b]**
ERCC5	rs17655	C/G	318	234	49	157	73	18	0.60 (0.43-0.82)	**0.018**	0.75 (0.40-1.39)	0.491	0.69 (0.53-0.89)	**0.046**
BRIP1	rs4986764	C/T	224	270	107	93	130	25	0.95 (0.69-1.31	0.809	0.48 (0.29-0.78)	**0.026**	0.82 (0.65-1.02)	0.157
DIFFUSE GC			**HC Genotype**			**GC Genotype**			**Dominant model**		**Recessive model**		**Log-Additive model**	
Gen	**db SNP ID**	**A/a**	**AA**	**Aa**	**aa**	**AA**	**Aa**	**aa**	**OR (95% CI)[a]**	**FDR[b]**	**OR (95% CI)[a]**	**FDR[b]**	**OR (95% CI)[a]**	**FDR[b]**
XRCC3	rs861528	G/A	350	205	33	66	73	13	2.11 (1.43-3.12)	0.001	1.75 (0.87-3.51)	**0.239**	1.75 (1.30-2.37)	0.003
XRCC3	rs861531	G/T	230	277	88	50	96	31	1.89 (1.26-2.84)	0.009	1.17 (0.72-1.89)	**0.685**	1.39 (1.07-1.81)	0.077
APEX1	rs1130409	T/G	155	300	145	62	78	38	0.61 (0.41-0.89)	0.044	0.76 (0.49-1.19)	**0.333**	0.74 (0.58-0.96)	0.078
TP53	rs1042522	G/C	314	247	40	113	53	12	0.64 (0.44-0.92)	0.046	1.01 (0.52-1.98)	**0.723**	0.77 (0.57-1.05)	0.185

HC, healthy control; GC, gastric cancer; A/a, major/minor alleles; OR, odds ratio; CI, confidence interval.
[a]ORs and 95% CIs were calculated by logistic regression analysis adjusted by gender, age, *H. pylori* infection, smoking, and family history of GC.
[b]Q_{FDR}-values obtained after applying the False Discovery Rate (FDR) test. Q_{FDR}-values < 0.05 are highlighted in bold.

identified *H. pylori* infection with CagA strains (OR: 1.99; 95% CI: 1.55–2.54), smoking habit (OR: 1.77; 95% CI: 1.22–2.57), and positive family history of GC (OR: 2.87; 95% CI: 1.85–4.45) as independent risk factors for the development of GC. Concerning genetic factors, the *LIG3* rs2074522 polymorphism was associated with a higher risk of GC (OR: 5.67; 95% CI: 1.24–25.95, recessive model) whereas the *TP53* rs9894946 (OR:0.73; 95% CI: 0.56–0.96, log-additive model), *TP53* rs1042522 (OR: 0.76; 95% CI: 0.56–0.96, dominant model), and *BRIP1* rs4986764 (OR: 0.55; 95% CI: 0.38–0.78, recessive model) variants were associated with a lower risk of developing the disease (Table 5).

DISCUSSION

Over the last few years, numerous studies concerning the association between DNA repair gene polymorphisms and GC risk have been conducted in different geographic areas and ethnic groups. However, most studies have yielded inconsistent and discrepant results [18, 19, 22, 23]. To assess the relevance of DNA repair gene polymorphisms to GC susceptibility and phenotype, we analyzed a total of 123 SNPs located in 52 genes involved in different DNA repair pathways.

In our population, four SNPs located in the *TP53* (rs1042522G>C, rs9894946G>A), *LIG3* (rs2074522G>A), and *BRIP1* (rs4986764C>T) genes were significantly associated with GC susceptibility after FDR multiple test correction. Thus, allele A of *LIG3* rs2074522 was associated with a higher risk of GC whereas the *TP53* rs9894946A, *TP53* rs1042522C, and *BRIP1* rs4986764T variants were associated with a lower risk of developing the disease. Interestingly, these four variants are located in the long (*LIG3* q11.2–q12, *BRIP1* q22.2) and short arms (*TP53* p.13.1) of chromosome 17, suggesting that this region of the genome represents a promising target for more extensive investigations in the field of GC research.

TP53 (tumor protein p53) is a tumor suppressor gene that encodes a potent nuclear transcription factor with a fundamental role in the maintenance of genomic stability. When activated in response to cellular stress, the p53 protein induces cell cycle arrest and apoptosis, inhibits cell growth, and interacts with proteins involved in DNA repair [24]. High frequencies of somatic mutations in the *TP53* gene and/or overexpression of p53 protein have been reported in many types of human cancers, including GC [25]. Although *TP53* is a highly polymorphic gene, the most explored polymorphism is a nonsynonymous SNP (rs1042522G>C) located in a proline–rich domain in

Table 4: DNA repair gene haplotypes associated with gastric cancer risk

Gene	SNPs	Haplotype	Frequency HC	Frequency GC	OR (95% CI)[a]	*P*-value
BRIP1	rs2048718	CAC	0.3730	0.4043	Reference	
	rs4968451	CAT	0.2021	0.1852	0.85 (0.65–1.1)	0.2203
	rs4986764	TAC	0.1622	0.1609	0.91 (0.69–1.20)	0.5112
		TCT	0.1117	0.0888	0.73 (0.53–0.99)	**0.0459**
		TCC	0.0621	0.0712	1.07 (0.71–1.62)	0.7384
ERCC4	rs1799801	TGCC	0.5944	0.6408	Reference	
	rs1800067	CGGT	0.1857	0.1666	0.83 (0.66–1.03)	0.0927
	rs2238463	CAGT	0.1167	0.1134	0.89 (0.69–1.16)	0.3962
	rs3136038	TGGT	0.0790	0.0599	0.70 (0.50–0.96)	**0.0291**
ERCC5	rs1047768	CC	0.5330	0.5460	Reference	
	rs17655	TG	0.2335	0.1908	0.80 (0.66–0.98)	**0.0350**
		TC	0.1908	0.2155	1.11 (0.89–1.37)	0.3500
TP53	rs1042522	GCG	0.4331	0.4417	Reference	
	rs1614984	GTG	0.2490	0.2939	1.13 (0.92–1.38)	0.2367
	rs9894946	CTG	0.1347	0.1180	0.88 (0.67–1.14)	0.3292
		CCA	0.1222	0.0847	0.68 (0.51–0.91)	**0.0081**

HC, healthy control; GC, gastric cancer; OR, odds ratio; CI, confidence interval.
Haplotypes with frequencies > 0.05 are shown in the table.
[a]Odds ratios and 95% confidence intervals were calculated according to the additive genetic model taking as a reference the more common haplotype.
P-values < 0.05 are highlighted in bold.

exon 4, which causes a proline–to–arginine substitution at codon 72 (Arg72Pro) [26]. Evidence indicates that this change in amino acid sequence affects the biochemical and biological functions of p53 [27], suggesting that the rs1042522 SNP may be relevant in cancer development. In this context, a number of case–control studies have reported the association of both the rs1042522G (Arg) and rs1042522C (Pro) variants with GC risk [28, 29]. Allele frequencies of rs1042522G>C differ notably among populations with values for the rs1042522C (Pro) variant ranging from ~63% in African Blacks to ~41% in Asians or ~17% in Swedish Saamis [30]. The relevance of these major ethnic and geographical variations in *TP53* rs1042522 profiles are supported by two recent meta–analyses showing a significant association between the rs1042522C (Pro) variant and GC in Eastern Asian populations but not in Caucasians and South Americans [31, 32]. Similarly, some opposing associations have been reported among ethnicities when considering the location and histological subtypes of GC [33, 34]. However, and as the authors note, the specific meta–analysis performed in Caucasians comprised very few studies, which were limited by sample size, differed in methodology, or lacked information about other well-documented risk factors for GC, such as *H. pylori* infection, tobacco smoking, and diet. In line with our results, Pérez-Pérez *et al*. [28] and Zhang *et al*. [32] observed a significantly lower frequency of the rs1042522C (Pro) allele in GC patients compared to HCs. Moreover, an Italian study by De Feo *et al*. [35] showed a significant interaction between both *TP53* rs1042522C and rs1625895A minor alleles and protection against GC.

The rs1042522 SNP is located in a proline–rich domain of the *TP53* gene, which is essential for the regulation of p53–mediated apoptosis. In this regard, Marin *et al*. [36] first reported the contribution of rs1042522 allele variants to the induction of apoptosis in p53 mutant cells. According to the authors, p53 mutants encoded by the rs1042522G (Arg) allele are preferentially selected during tumorigenesis because they prevent tumor cells from apoptotic cell death. Moreover, Schneider-Stock *et al.* [37] demonstrated that the rs1042522C (Pro) allele induces FasL/Fas–mediated apoptosis of tumor cells by cytotoxic T lymphocytes more effectively than does the rs1042522G (Arg) allele. Taken together, these results indicate a positive association between rs1042522G (Arg)

Table 5: Logistic regression analysis environmental and genetic factors associated with GC risk

Factor	OR	(95% CI)	*P*-value
Gender	0.98	(0.72–1.33)	0.892
Age	1.00	(0.99–1.01)	0.533
Infection with *H. pylori* CagA+	1.99	(1.55–2.54)	**0.000**
Tobacco (being current smoker)	1.77	(1.22–2.57)	**0.003**
Positive family history of GC	2.87	(1.85–4.45)	**0.000**
TP53 rs1042522 allele C (dominant model)	0.76	(0.58–0.98)	**0.043**
TP53 rs9894946 allele A (log-additive model)	0.73	(0.56–0.96)	**0.027**
LIG3 rs2074522 allele A (recessive model)	5.67	(1.24–25.95)	**0.025**
BRIP1 rs4986764 allele T (recessive model)	0.55	(0.38–0.78)	**0.001**

GC, gastric cancer; OR, odds ratio; 95% CI, 95% confidence interval.
P- values < 0.05 are highlighted in bold.

status and reduction of apoptotic tumor cell death, an inference that is in line with the association of the *TP53* rs1042522C (Pro) variant and lower risk of GC observed in our population.

A second polymorphism in the *TP53* gene (rs9894946G>A), located in intron 10, was identified as a protective factor for GC development in our population. In line with these findings, Sprague *et al*. [38] reported a ~40% reduction in invasive breast cancer risk among women < 50 years carrying the rs9894946A allele. However, two other studies by García-Closas *et al*. [39] and Schildkraut *et al*. [40] found no evidence of association for rs9894946 and cancer development. Although variations in intronic structure have been proposed to influence cancer susceptibility via regulation of gene expression, gene splicing, or mRNA stability [41], the functional relevance of rs9894946 for p53 expression or function is still unknown. It is also plausible that this intronic polymorphism is in LD with other functional SNPs that may affect cancer risk. In our study, the *TP53* rs1042522 and rs9894946 variants showed a moderate LD ($D' = 0.63$, $r^2 = 0.22$). Haplotype analysis did not provide additional information beyond individual SNP results, and haplotype *TP53* rs1042522C, rs1614984C, rs9894946A, containing both rs1042522C and rs9894946A protective alleles, was inversely associated with GC risk in our population. To our knowledge, this is the first study reporting the link between rs9894946 and risk of GC. Therefore, further studies with larger populations and different ethnic groups are required to conclusively assess the relevance of this SNP for GC development.

As noted, the nonsynonymous rs4986764C>T polymorphism (S919P) located in exon 18 of the *BRIP1* gene was associated with a lower risk of GC in our study. The *BRIP1* (BRCA1-interacting protein 1) gene encodes a DEAH-box DNA helicase that directly interacts with the C–terminal domain of *BRCA1*. This bound complex is crucial for the normal double–strand break repair function of BRCA1 and checkpoint functions [42]. The *BRIP1* rs2048718, rs4986764, and rs4968451 SNPs, all evaluated in our study, have been associated with susceptibility to meningioma [43], breast, and ovarian cancer [44]. However, no previous studies have addressed the contribution of *BRIP1* gene variants to GC risk. In line with our results, Ma *et al*. [45] reported a protective effect of the rs4986764T allele against cervical cancer in a Chinese Han population, and individuals carrying the rs11079454T–rs4986763T–rs4986764T haplotype were less prone to cervical cancer. The same authors demonstrated that BRIP1 mRNA levels correlated with rs4986764 genotypes [46]. Based on the major anti–oncogenic role of the *BRIP1* pathway, a low–level BRIP1 activation associated with the rs4986764C allele may lead to cancer development through an impaired DNA repair process. The scarcity of *BRIP1* association studies highlights the need to characterize the genetic variation defined by the rs4986764 SNP and the functional consequences affecting BRIP1 expression or protein function.

Similar to *BRIP* variants, knowledge is very limited about the influence of *LIG3* (DNA ligase 3) gene polymorphisms to GC cancer susceptibility. *LIG3* is one of three mammalian genes encoding DNA ligases I, III, and IV. These proteins catalyze the joining of DNA ends although they each have a distinct functional significance [47]. DNA Lig III participates in the BER pathway and DNA single strand break repair by forming a stable complex with XRCC1. Polymorphisms in the *LIG3* gene have been associated with increased risk of several cancers such as colon [48], lung [49], and esophageal cancer [50]. In the present study, the rare allele A of the intronic rs2074522 variant (MAF: 0.089) was significantly associated with a higher overall risk of GC. In contrast

with our findings, patients homozygous for the rs2074522 A allele were less prone to developing pancreatic cancer in a US study by Li *et al*. [51]. In addition to tissue–specific factors, these discrepant results could be explained by the low frequency of the rs2074522 AA genotype among Caucasians. In our population, the frequencies of the rs2074522 AA genotype in healthy individuals (0.33%) and GC patients (2.15%) were similar to those reported in European populations. Therefore, although Q_{FDR} values for *LIG3* rs2074522 retained significance in several genetic models, our results should be interpreted with caution and confirmed in future studies with larger sample sizes.

Stratified SNP analysis by tumor location (cardia/non–cardia) and histological type of GC (intestinal/diffuse) revealed some additional significant associations. Of interest, three SNPs (rs1799801T>C, rs2238463C>G, and rs3136038C>T) located in the NER gene *ERCC4* (excision repair cross-complementary group 4) and in strong LD with each other were inversely associated with cardia GC risk. The *ERCC4* gene, also known as *XPF*, is a key component of the NER pathway that also plays an important role in removal of DNA interstrand cross–links and DNA double-strand breaks [52]. Information concerning the relevance of *ERCC4* gene variants to GC susceptibility is very limited. To date, only studies performed in Asians have been published. Two Chinese reports by Gong *et al*. [53] and He *et al*. [54] found no association between risk of GC and rs6498486T>G, a tag SNP located in the promoter region which tags the rs3136038 SNP evaluated in our study. Similarly, Zhang *et al*. [55] observed a non–significantly decreased risk in patients carrying the rs180067 G or rs1799801 T alleles. In agreement with these results, we found no significant associations between *ERCC4* variants and overall risk of GC after FDR multiple test corrections. However, carriers of the minor rs1799801C, rs2238463G, or rs3136038T alleles had a significantly lower risk of developing cardia GC. Functional studies by Shi *et al*. [56] reported higher XPF transcript expression levels in subjects carrying the rs1799801 CC genotype compared to those carrying the wild T allele, a finding that is biologically plausible with the protective effect of the rs1799801 C variant observed in our study.

When considering the histological type of tumor, the most remarkable associations were observed in the DSBR gene *XRCC3* (X-ray repair cross complementing 3), with the rs861528G>A and rs861531G>T intronic variants being associated with a higher risk of diffuse GC. The *XRCC3* gene encodes a member of the RecA/Rad51–related protein family that functions in homologous recombination repair of DNA double–strand breaks [57]. The most explored polymorphism is a C>T transition in exon 7 (rs861539), which causes a threonine–to–methionine substitution at codon 241 (Thr241Met) [58]. In agreement with a recent meta–analysis [59], we found no evidence of association for rs861539 and GC risk. However, FDR values (Q_{FDR} = 0.054) showed a borderline increased risk of diffuse GC in patients carrying the T allele. Unlike rs861539, very few studies have been published on rs861528/rs861531 variants and cancer susceptibility, most of them reporting inconclusive results. In the current work, rs861528 and rs861531 showed a moderate–high LD (D′ = 0.97, r^2 = 0.55). Of interest, the rs861531 SNP was highly linked with the functional rs861539 Thr241Met variant (D’ = 0.99, r^2 = 0.94), with lower values for rs861528 and rs861539 (D’ = 0.90, r^2 = 0.47). Despite the potential influence of intronic variants in gene regulation, the functional relevance of the susceptible intronic rs861528 and rs861531 SNPs remains unknown. Taken together, these major differences in genotype distribution and environmental exposures observed in our study among GC subtypes reveal the marked heterogeneity of GC and highlight the need to investigate each type separately when possible. Because GC subtypes may result from different pathogenic mechanisms, this strategy of refining the phenotype may improve power for detecting genetic associations.

Finally, we also examined whether the contribution of DNA repair genes to GC risk could be modified by other risk factors identified in our study, such as *H. pylori* infection, smoking, and positive family history of GC. Whereas smoking and family history of GC showed no effect in modifying the contribution of DNA repair polymorphisms to GC, a significant association between the previously reported *TP53* rs1042522, rs9894946, *LIG3* rs2074522, and *BRIP1* rs4986764 variants and overall GC risk was observed among *H. pylori* infected patients. After FDR correction, only *TP53* rs1042522 (P72R) remained significant, although tests for interaction between rs1042522 and *H. pylori* infection did not reach statistical significance. Taking into account that none of the SNPs analyzed in our study were associated with prevalence of infection or CagA/VacA strains, our findings suggest that *TP53* rs1042522 is likely to be associated with GC development after bacterial infection occurs and not with susceptibility to *H. pylori* infection *per se*. In this context, mutants of p53 protein have been recently reported as potential markers of *H. pylori*–associated gastric carcinogenesis [60]. Moreover, inflammation induced by *H. pylori* infection results in the generation of DNA–damaging reactive oxygen and nitrogen species in gastric epithelial cells [61]. Under normal conditions, there is a balance between DNA damage and DNA repair; however, reduced DNA repair capacity associated with gene variants and increased DNA damage generated by *H. pylori* infection may alter this status and give rise to the accumulation of DNA damage and consequently cancer development. Unfortunately, the scarcity of studies [53, 62, 63] addressing this issue makes it very difficult to conclude whether *H. pylori* infection has any effect on the relationship between DNA repair gene variants and GC risk.

Our study has several strengths and limitations. A comprehensive analysis of 123 SNPs in candidate DNA repair genes, some of them not previously evaluated for the risk of GC, was carried out in a homogeneous population of Spanish Caucasian subjects (603 HCs and 603 GC patients). To our knowledge, the current study is the first to show a significant effect of *TP53* rs9894946, *LIG3* rs2074522, and *BRIP1* rs4986764 variants on GC susceptibility. Moreover, additional associations with specific anatomic locations and histological subtypes of GC were observed. The fact that these associations remained significant after FDR multiple test corrections indicates that our results may not be a chance finding. However, some limitations also should be considered. In particular, although our study is one of the largest performed in Western populations, the sample size limited the power to detect small ORs, mainly in low–frequency variant polymorphisms. Taking into account the prevalence of the SNPs evaluated in our population and setting an a value of 0.05, the study had a power of 85% to detect ORs > 1.45 or < 0.70 except for the less prevalent variants (MAF: 0.05–0.10), with a power of 80% to observe OR > 1.97 in the whole data set. As a result, it is possible that we could have missed minor statistical differences, especially when subgroup analyses and assessment of gene–environment interactions were performed.

In summary, we can conclude that the *TP53* (rs1042522, rs9894946G), *LIG3* (rs2074522G), and *BRIP1* (rs4986764) variants are involved in the susceptibility to GC, particularly in subjects infected by *H. pylori*. Like many other complex diseases, GC is the result of a multifactorial interplay involving environmental, lifestyle, and host genetic factors. Because the magnitude of each etiologic factor might differ among populations, larger studies in different geographic areas and ethnic groups are warranted to elucidate the contribution of DNA repair gene polymorphisms and their interactions with other risk factors in the susceptibility to GC and phenotype.

MATERIALS AND METHODS

Subjects

A total of 684 Spanish Caucasian patients with primary GC diagnosed in a network of 16 general hospitals in Spain, from May 2003 to December 2010, were invited to take part in the study. Patients with gastric neoplasms other than adenocarcinoma, secondary or recurrent GC, previous history of other malignancies, or refusal to participate were excluded. Finally, 646 GC patients were initially selected as cases for this study. Gastric tumors were classified according to their histological type [3] as intestinal, diffuse, or indeterminate, and by anatomical location as proximal and non–cardia or distal GC. Information regarding demographic characteristics and potential risk factors including smoking habits and family history of GC were collected by a questionnaire administered by trained personnel as previously described [64].

The control group consisted of 646 Spanish, Caucasian, cancer–free volunteers with no previous history or symptoms of gastrointestinal disease, matched by gender, age (±5 years), and area of residence. Most controls were blood donors and individuals recruited from the outpatient clinical services in the same hospitals as cases. Eligible controls were also interviewed with the same standard questionnaire designed for patients.

Following completion of the interview, 10 ml of peripheral blood was collected from each participant for DNA extraction and serological study of *H. pylori* infection. Once processed, whole blood and serum samples were aliquoted and stored at –80°C until analysis. All patients and controls gave written informed consent to the study protocol, which was approved by the Ethical Committee of the Hospitals.

Helicobacter pylori diagnosis

The presence of *H. pylori* infection was determined in GC patients by urease test (CLO-test; Delta West Ltd., Canning Vale, Bentley, Australia) and histological examination of biopsies taken at the antrum and corpus of the stomach during the endoscopic procedure. In addition, GC patients and controls were analyzed to determine in serum the presence of *H. pylori* infection and antibodies to CagA and/or to VacA antigens by western blot analysis (Bioblot Helicobacter, Izasa, Barcelona, Spain). This test for *H. pylori* infection and CagA/VacA antibodies has been previously validated in our area [65]. GC patients were considered positive for bacterial infection if any of the three tests was positive. However, for statistical and data analysis, only information related to western blot analysis in serum samples from CG patients and controls was considered.

SNP selection and genotyping

All DNA repair gene polymorphisms evaluated in our study were selected from the NCBI data base (http://www.ncbi.nlm.nih.gov/snp), Genome build 38.p2. The panel of SNPs was chosen based on three criteria: (1) a reported prevalence of at least 5% for the less frequent allele among Caucasians; (2) potential functional consequences or (3) published evidence of an association with different types of cancer. We assessed a total of 123 SNPs located in 52 genes related to different DNA repair pathways (Supplementary Table 12). The selected panel comprised 18 SNPs located in genes involved in BER genes (*PARP1*, *OGG1*, *POLB*, *POLG*, *POLI*, *FEN1*, *APEX1*, *NEIL1*, *LIG1*, *LIG3*, *XRCC1*, *PCNA*), 26 SNPs located in NER genes (*ERCC1*, *ERCC2*, *ERCC3*, *ERCC4*, *ERCC5*, *ERCC6*, *XPA*, *XPC*, *POLE*), 29 SNPs located

in MMR genes (*MUTHY*, *EXO1*, *MSH2*, *MSH3*, *MSH6*, *MLH1*, *MLH3*, *PMS2*), 38 SNPs located in DSBR genes by homologous recombination (*XRCC2*, *XRCC3*, *BRCA1*, *BRCA2*, *BRIP1*, *RAD51*, *RAD51B*, *RAD52*, *RAD54L*, *MRE11A*) or non–homologous end joining (*XRCC4*, *XRCC5*, *XRCC6*, *RAD50*, *WRN*, *NES1*, *LIG4*), 8 SNPs located in cell cycle checkpoint genes (*ATM*, *ATR*, *TP53*), and 4 SNPs located in genes (*MGMT*, *ALKBH2*, *ALKBH3*) coding for proteins involved in direct repair of DNA damage produced by alkylating agents.

Genomic DNA from patients and controls was extracted from ethylenediamine-tetraacetic acid–preserved whole blood using the QIAamp DNA Blood Mini extraction kit (Qiagen, Izasa, Barcelona, Spain). Genotyping was performed at the Spanish National Genotyping Centre (CEGEN-Santiago de Compostela) using the Illumina Veracode Platform (Illumina, Eindhoven, The Netherlands). As a quality control, 5% of samples, including internal controls by CEGEN, were analyzed in duplicate with a concordance rate of 100% for all assays. Among the 123 SNPs evaluated, 15 SNPs were excluded from the analysis due to failure of genotyping (*MUTYH* rs3219484, *MSH2* rs2303426, *ATR* rs2227928, *MSH3* rs184967, *ERCC6* rs2228526, *POLE* rs5744751, *RAD51B* rs10483813, *XRCC1* rs25489, *ERCC1* rs11615, *XRCC6* rs132788), SNP call rate < 90% (*BRCA1* rs3737559, *MSH2* rs1863332, *ERCC6* rs2228524, *MGMT* rs12917), or monomorphism (*POLB* rs12678588). Samples in which more than 20% of the SNPs failed genotyping were excluded (cases = 29, HCs = 15). In this study, genotype completion on genomic DNA samples exceeded 95%. Finally, after excluding 42 unmatched samples, 108 SNPs in 1206 subjects (603 GC patients and 603 HCs) were successfully genotyped and available for analysis.

Statistical analysis

Genotype frequencies for each DNA repair gene polymorphism among controls were tested for Hardy–Weinberg equilibrium by a Chi-square (χ^2) test with one degree of freedom (Supplementary Table 12). Genotype and allele frequencies between CG patients and controls were compared using the χ^2 test with Yates' correction or Fisher's exact test. The magnitude of the association of each polymorphism was estimated by ORs and 95% CIs using the *SNPassoc* package implemented in R. Analyses were performed using codominant, dominant, recessive, and log-additive genetic models. In addition, unconditional logistic regression analysis was conducted to quantify the influence of both genetic and environmental factors for GC as dependent variable. A variable was entered in the model if the significance level of its coefficient was less than 0.05 and was removed if it was greater than 0.10. Categorical variables included in the model were codified as dummy variables. For all tests, a two–sided *P* value < 0.05 was considered statistically significant. To address the issue of adjustment for multiple testing, the FDR test using a Benjamini–Hochberg method was applied [66]. Finally, comparison of common haplotype frequencies (> 0.05) in each gene block between GC patients and controls was performed. Estimated haplotype frequencies and LD coefficients (D´ and r^2) were calculated using the *haplo.stats* package implemented in R. For each marker, the more common haplotype was used as the reference category. The statistical analyses were performed using SPSS 23.0 for Windows (SPSS Ibérica, Madrid, Spain).

Taking into account the prevalence of the analyzed SNPs in our population, the size of the study was sufficient to detect ORs > 1.45 or < 0.70 with a power of 80% and a a value of 0.05. For the less prevalent polymorphisms (MAF: 0.05–0.10), the study had a power of 80% to detect an OR of > 1.97 in the whole data set. All power calculations were performed using the program Epidat 4.1.

Abbreviations

ALKBH2: alkB homolog 2, alpha-ketoglutarate dependent dioxygenase. *ALKBH3*: alkB homolog 3, alpha-ketoglutarate dependent dioxygenase. *APEX1*: apurinic/apyrimidinic endodeoxyribonuclease 1. *ATM*: ATM serine/threonine kinase. ATR: ATR serine/threonine kinase. *BRCA1*: BRCA1, DNA repair associated. *BRCA2*: BRCA2, DNA repair associated. *BRIP1*: BRCA1 interacting protein C-terminal helicase 1. *ERCC1*: ERCC excision repair 1, endonuclease non-catalytic subunit. *ERCC2*: ERCC excision repair 2, TFIIH core complex helicase subunit. *ERCC3*: ERCC excision repair 3, TFIIH core complex helicase subunit. *ERCC4*: ERCC excision repair 4, endonuclease catalytic subunit. *ERCC5*: ERCC excision repair 5, endonuclease. *ERCC6*: ERCC excision repair 6, chromatin remodeling factor. *EXO1*: exonuclease 1. *FEN1*: flap structure-specific endonuclease 1. *LIG1*: DNA ligase 1. *LIG3*: DNA ligase 3. *LIG4*: DNA ligase 4. *MGMT*: O-6-methylguanine-DNA methyltransferase. MLH1: mutL homolog 1. MLH3: mutL homolog 3. *MRE11A*: MRE11 homolog, double strand break repair nuclease. *MSH2*: mutS homolog 2. *MSH3*: mutS homolog 3. *MSH6*: mutS homolog 6. *MUTYH*: mutY DNA glycosylase. NBS1: nibrin. *NEIL1*: nei like DNA glycosylase. *OGG1*: 8-oxoguanine DNA glycosylase. *PARP1:* poly(ADP-ribose) polymerase 1. *PCNA*: proliferating cell nuclear antigen. *PMS2*: PMS1 homolog 2, mismatch repair system component. *POLB*: DNA polymerase beta. *POLE*: DNA polymerase epsilon, catalytic subunit. *POLG*: DNA polymerase gamma, catalytic subunit. POLI: DNA polymerase iota. RAD50: RAD50 double strand break repair protein. RAD51B: RAD51 paralog B. RAD52: RAD52 homolog, DNA repair protein. RAD54L: RAD54-like. TP53: tumor protein p53. WRN: Werner syndrome RecQ like helicase. XPA: XPA, DNA damage recognition and repair factor. XPC: XPC complex subunit, DNA damage recognition and repair

factor. XRCC1: X-ray repair cross complementing 1. XRCC2: X-ray repair cross complementing 2. XRCC3: X-ray repair cross complementing 3. XRCC4: X-ray repair cross complementing 4. XRCC5: X-ray repair cross complementing 5. XRCC6: X-ray repair cross complementing 6.

Authors' contributions

Patricia Carrera-Lasfuentes: involved in statistical analysis, interpretation of data, and drafting/editing the manuscript. Angel Lanas, Luis Bujanda, Enrique Quintero: involved in data collection, interpretation of data, and drafting/editing the manuscript. Mark Strunk: involved in DNA isolation, supervision of DNA genotyping, statistical analysis, and interpretation of data. Rafael Benito: involved in performance of serological determination of CagA/VacA antibodies, analysis and interpretation of data. Santos Santolaria, Federico Sopeña, Elena Piazuelo, Concha Thomson, Angeles Pérez-Aisa, David Nicolás-Pérez, Elizabeth Hijona, Jesús Espinel, Rafael Campo, Marisa Manzano, Fernando Geijo, María Pellise, Manuel Zaballa, Ferrán González-Huix, Jorge Espinós, Llúcia Titó, Luis Barranco, and Mauro D'Amato: involved in patient enrollment, sample collection, and acquisition of data. Mª Asunción García-González: involved in the study design, planning, conducting, interpretation of data, and drafting/editing the manuscript. All the above–mentioned authors have approved the final draft submitted.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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Relevance of DNA repair gene polymorphisms to gastric cancer risk and phenotype

Supplementary Materials

Supplementary Table 1: Demographic and clinical characteristics of HCs and GC patients according to the location and histological type of tumor

	Healthy Controls *n* = 603	Cardia GC *n* = 117	ORs (95% CI)	*P* Value	Non–Cardia GC *n* = 486	ORs (95% CI)	*P* Value
Age yrs ± SD (range)	70.17 ± 12.32 (30–96)	69 ± 11.06 (30–91)	0.99 (0.98–1.01)	0.67	70.59 ± 12.55 (30–96)	1 (0.99–1.01)	0.69
Gender	413 M (68.5%)	102 M (87.2%)			311 M (64%)		
	190 F (31.5%)	15 F (12.8%)	3.15 (1.78–5.57)	**< 0.0001**	175 F (36%)	0.83 (0.64–1.07)	0.14
Cigarette smoking							
Never	311/585 (53.2%)	33/114 (28.9%)	Reference		258/468 (55.1%)	Reference	
Former	184/585 (31.4%)	53/114 (46.5%)	2.71 (1.69–4.35)	**< 0.0001**	101/468 (21.6%)	0.71 (0.53–0.95)	**0.02**
Current smoker	90/585 (15.4%)	28/114 (24.6%)	2.93 (1.68–5.11)	**0.0002**	109/468 (23.3%)	1.35 (0.97–1.88)	0.07
H. pylori +	364 (60.4%)	67/109 (61.5%)	1.01 (0.72–1.44)	0.93	310/447 (69.3%)	1.49 (1.15–1.94)	**0.002**
CagA+	253 (41.9%)	45/109 (41.3%)	0.97 (0.68–1.32)	0.96	280/447 (62.6%)	2.32 (180–2.98)	**< 0.0001**
VacA+	237 (39.3%)	38/109 (34.9%)	0.82 (0.54–1.27)	0.39	185/447 (41.4%)	1.09 (0.85–1.40)	0.49
Family history of GC	33/539 (6.1%)	12/104 (11.5 %)	1.42 (0.68–3.01)	0.42	76/430 (17.7%)	3.29 (2.14–5.06)	**< 0.0001**
	Healthy Controls *n* = 603	**Intestinal GC *n* = 250**	**ORs (95% CI)**	***P* Value**	**Diffuse GC *n* = 178**	**ORs (95% CI)**	***P* Value**
Age yrs ± SD (range)	70.17 ± 12.32 (30–96)	72.82 ± 10.73 (33–92)	1.02 (1.01–1.03)	**0.004**	67.34 ± 14.32 (30–96)	0.98 (0.98–0.99)	**0.005**
Gender	413 M (68.5%)	167 M (66.8%)			101 M (56.7%)		
	190 F (31.5%)	83 F (33.2%)	0.98 (0.72–1.36)	0.94	77 F (43.3%)	0.58 (0.41–0.82)	0.002
Cigarette smoking							
Never	311/585 (53.2%)	134/240 (55.8%)	Reference		102/171 (59.6%)	Reference	
Former	184/585 (31.4%)	65/240 (27.1%)	0.82 (0.58–1.16)	0.29	40/171 (23.4%)	0.66 (0.44–1.00)	0.06
Current smoker	90/585 (15.4%)	41/240 (17.1%)	1.06 (0.69–1.61)	0.83	29/171 (17%)	0.98 (0.61–1.58)	1
H. pylori +	364 (60.4%)	158/231 (68.4%)	1.47 (1.06–2.03)	**0.02**	123/159 (77.3%)	2.17 (1.44–3.26)	**< 0.0001**
CagA+	253 (41.9%)	143/231 (61.9%)	2.25 (1.65–3.07)	**< 0.0001**	109/159 (68.5%)	3.02 (2.08–4.37)	**< 0.0001**
VacA+	237 (39.3%)	100/231 (43.3%)	1.21 (0.88–1.64)	0.23	68/159 (42.8%)	1.11 (0.78–1.59)	0.56
Family history of GC	33/539 (6.1%)	42/222 (18.9%)	3.58 (2.20–5.82)	**< 0.0001**	23/159 (14.5%)	2.60 (1.47–4.56)	**0.001**

HCs, healthy controls; GC, gastric cancer; n, number of individuals; OR, odds ratio; CI, confidence interval; SD, standard deviation; M, male; F, female. OR and 95% CI values adjusted by sex and age. *P* values < 0.05 are highlighted in bold.

Supplementary Table 2: Genotype frequencies of DNA repair gene polymorphisms in gastric cancer patients and healthy controls.

			Healthy Controls n = 603					Gastric Cancer patients n = 603					Anatomic location								Histological type							
													Cardia GC n = 117				Distal GC n = 486				Intestinal GC n = 250				Diffuse GC n = 178			
db SNP ID	Gene	A/a	AA	Aa	aa	N	MAF	AA	Aa	aa	N	MAF	AA	Aa	aa	MAF	AA	Aa	aa	MAF	AA	Aa	aa	MAF	AA	Aa	aa	MAF
rs10079641	*MSH3*	C/G	472	117	4	593	0.105	473	110	6	589	0.104	94	22	—	0.095	379	88	6	0.106	195	47	3	0.108	139	33	2	0.106
rs1042522	*TP53*	G/C	314	247	40	601	0.272	372	192	39	603	0.224	70	43	4	0.218	302	149	35	0.225	150	80	20	0.240	113	53	12	0.216
rs1047768	*ERCC5*	C/T	204	284	113	601	0.424	221	274	108	603	0.406	47	50	20	0.385	174	224	88	0.412	95	106	49	0.408	61	89	28	0.407
rs1047840	*EXO1*	G/A	217	290	94	601	0.398	232	273	84	589	0.374	42	57	16	0.387	190	216	68	0.371	100	114	29	0.354	66	78	30	0.397
rs1048771	*RAD54L*	C/T	465	125	5	595	0.113	413	108	10	531	0.121	88	18	1	0.093	325	90	9	0.127	160	53	5	0.144	121	29	4	0.120
rs1051677	*XRCC5*	T/C	500	98	4	602	0.088	487	113	2	602	0.097	94	23	—	0.098	393	90	2	0.097	201	46	2	0.100	146	32	—	0.090
rs1051685	*XRCC5*	A/G	493	98	10	601	0.098	489	110	4	603	0.098	90	27	—	0.115	399	83	4	0.094	201	47	2	0.102	149	27	2	0.087
rs1052133	*OGG1*	C/G	367	210	26	603	0.217	381	195	27	603	0.206	74	37	6	0.209	307	158	21	0.206	153	83	14	0.222	118	53	7	0.188
rs1059262	*ALKBH2*	T/G	398	181	22	601	0.187	417	162	23	602	0.173	81	30	6	0.179	336	132	17	0.171	174	66	10	0.172	129	43	5	0.150
rs1060915	*BRCA1*	T/C	272	268	62	602	0.326	248	291	62	601	0.345	44	61	12	0.363	204	230	50	0.341	107	115	26	0.337	73	91	14	0.334
rs11226	*RAD52*	C/T	211	281	96	588	0.402	165	253	112	530	0.450	28	56	23	0.477	137	197	89	0.443	74	99	45	0.433	42	79	33	0.471
rs1130409	*APEX1*	T/G	155	300	145	600	0.492	180	282	139	601	0.466	33	53	30	0.487	150	229	106	0.455	75	121	53	0.456	62	78	38	0.433
rs1136410	*PARP1*	T/C	459	138	6	603	0.124	438	154	11	603	0.146	85	30	2	0.145	353	124	9	0.146	187	56	7	0.140	122	54	2	0.163
rs13180316	*XRCC4*	G/A	317	237	43	597	0.271	324	223	50	597	0.271	63	42	12	0.282	261	181	38	0.268	136	89	21	0.266	85	75	16	0.304
rs13181	*ERCC2*	T/G	275	254	74	603	0.333	258	261	83	602	0.355	52	43	22	0.372	206	218	61	0.351	108	107	34	0.351	75	80	23	0.354
rs1346044	*WRN*	T/C	360	207	34	601	0.229	374	202	22	598	0.206	79	33	3	0.170	295	169	19	0.214	158	85	6	0.195	104	64	9	0.232
rs144848	*BRCA2*	T/G	305	256	39	600	0.278	295	256	50	601	0.296	59	49	9	0.286	236	207	41	0.299	111	116	23	0.324	94	68	14	0.273
rs1478485	*XRCC4*	C/T	221	285	95	601	0.395	196	312	94	602	0.415	39	56	22	0.427	157	256	72	0.412	78	135	37	0.418	61	94	22	0.390
rs1540354	*MLH1*	T/A	469	120	13	602	0.121	478	111	11	600	0.111	95	20	2	0.103	383	91	9	0.113	192	50	6	0.125	144	30	3	0.102
rs1614984	*TP53*	C/T	227	273	88	588	0.382	183	252	90	525	0.411	31	57	18	0.439	152	195	72	0.405	72	97	44	0.434	62	69	23	0.373
rs1618536	*ERCC2*	G/A	162	264	155	581	0.494	155	245	124	524	0.470	30	52	25	0.477	125	193	99	0.469	60	101	52	0.481	46	72	34	0.461
rs1650697	*MSH3*	C/T	322	221	44	587	0.263	307	185	37	529	0.245	53	47	7	0.285	254	138	30	0.235	134	72	12	0.220	91	50	12	0.242
rs174538	*FEN1*	G/A	289	242	57	588	0.303	259	214	51	524	0.302	45	53	9	0.332	214	161	42	0.294	116	83	17	0.271	73	61	16	0.310
rs175080	*MLH3*	G/A	198	281	120	599	0.435	186	293	116	595	0.441	34	63	20	0.440	152	230	96	0.441	74	127	47	0.446	61	78	36	0.429
rs1760944	*APEX1*	C/A	212	271	72	555	0.374	207	253	75	535	0.377	37	49	15	0.391	170	204	60	0.373	84	117	24	0.367	56	68	29	0.412
rs17655	*ERCC5*	C/G	318	234	49	601	0.276	350	214	36	600	0.238	68	45	4	0.226	282	169	32	0.241	157	73	18	0.220	95	73	10	0.261
rs176641	*POLG*	A/C	262	266	75	603	0.345	221	302	79	602	0.382	51	49	17	0.355	170	253	62	0.389	88	130	31	0.386	62	99	17	0.374
rs1776148	*EXO1*	G/A	227	282	91	600	0.387	223	295	82	600	0.382	45	56	15	0.371	178	239	67	0.385	95	122	33	0.376	54	95	27	0.423
rs1799793	*ERCC2*	G/A	292	249	62	603	0.309	277	252	73	602	0.331	58	40	19	0.333	219	212	54	0.330	113	110	26	0.325	81	76	21	0.331
rs1799794	*XRCC3*	A/G	334	225	42	601	0.257	342	224	34	600	0.243	67	44	6	0.239	275	180	28	0.244	144	86	19	0.249	100	72	4	0.227
rs1799796	*XRCC3*	A/G	338	230	31	599	0.244	359	217	27	603	0.225	72	39	6	0.218	287	178	21	0.226	142	99	9	0.234	112	56	10	0.213
rs1799801	*ERCC4*	T/C	280	261	59	600	0.316	306	239	57	602	0.293	71	35	11	0.244	235	204	46	0.305	118	106	25	0.313	85	78	15	0.303
rs1799955	*BRCA2*	A/G	358	218	27	603	0.226	354	230	18	602	0.221	66	47	4	0.235	288	183	14	0.218	152	91	6	0.207	102	71	5	0.228
rs1799966	*BRCA1*	A/G	267	271	65	603	0.333	244	291	60	595	0.345	44	62	11	0.359	200	229	49	0.342	104	114	26	0.340	73	90	14	0.333
rs1799977	*MLH1*	A/G	272	258	73	603	0.335	265	278	60	603	0.330	41	58	18	0.402	224	220	42	0.313	107	121	22	0.330	91	74	13	0.281
rs1800067	*ERCC4*	G/A	458	129	7	594	0.120	465	124	6	595	0.114	97	19	1	0.090	368	105	5	0.120	187	54	3	0.123	135	40	1	0.119
rs1800389	*WRN*	T/C	328	224	49	601	0.268	347	211	40	598	0.243	65	46	5	0.241	282	165	35	0.244	146	81	21	0.248	100	63	14	0.257
rs1800734	*MLH1*	G/A	349	210	40	599	0.242	341	218	37	596	0.245	71	38	7	0.224	270	180	30	0.250	141	93	11	0.235	98	65	14	0.263
rs1800935	*MSH6*	T/C	310	244	43	597	0.276	282	276	42	600	0.300	54	55	8	0.303	228	221	34	0.299	116	110	22	0.310	87	79	12	0.289

rs1800975	*XPA*	G/A	282	256	65	603	0.320	296	248	59	603	0.303	47	50	20	0.385	249	198	39	0.284	128	102	20	0.284	96	69	13	0.267
rs1801406	*BRCA2*	A/G	284	264	55	603	0.310	284	283	32	599	0.290	52	58	7	0.308	232	225	25	0.285	122	113	13	0.280	80	88	8	0.295
rs1801516	*ATM*	G/A	447	146	9	602	0.136	433	157	12	602	0.150	84	31	2	0.150	349	126	10	0.151	174	68	7	0.165	126	49	3	0.154
rs1802904	*ATR*	A/G	459	138	6	603	0.124	446	140	13	599	0.139	85	30	2	0.145	361	110	11	0.137	176	68	5	0.157	138	33	5	0.122
rs1805386	*LIG4*	T/C	412	173	15	600	0.169	415	172	13	600	0.165	79	31	7	0.192	336	141	6	0.158	169	77	3	0.167	130	44	3	0.141
rs1805388	*LIG4*	C/T	442	136	10	588	0.133	383	131	11	525	0.146	68	33	3	0.188	315	98	8	0.135	157	56	5	0.151	121	28	3	0.112
rs1805794	*NBS1*	C/G	310	233	59	602	0.292	300	241	61	602	0.301	51	53	12	0.332	249	188	49	0.294	140	81	29	0.278	91	71	16	0.289
rs1981928	*MSH2*	T/A	315	241	45	601	0.275	307	258	34	599	0.272	56	51	10	0.303	251	207	24	0.265	128	108	11	0.263	90	76	11	0.277
rs2020911	*MSH6*	A/T	253	268	80	601	0.356	255	274	74	603	0.350	43	60	14	0.376	212	214	60	0.344	106	112	32	0.352	74	80	24	0.360
rs2040639	*XRCC2*	G/A	175	291	133	599	0.465	194	284	117	595	0.435	35	56	24	0.452	159	228	93	0.431	79	120	47	0.435	58	81	37	0.440
rs2048718	*BRIP1*	C/T	189	282	105	576	0.427	202	281	100	583	0.413	44	56	9	0.339	158	225	91	0.429	79	117	45	0.429	56	85	34	0.437
rs20580	*LIG1*	C/A	171	286	143	600	0.477	155	295	150	600	0.496	29	59	28	0.496	127	236	121	0.494	68	124	56	0.476	51	84	43	0.478
rs2074522	*LIG3*	G/A	509	89	2	600	0.078	496	94	13	603	0.100	103	13	1	0.064	393	81	12	0.108	207	38	5	0.095	145	30	3	0.101
rs2075685	*XRCC4*	G/T	193	296	113	602	0.434	174	319	109	602	0.446	32	61	24	0.466	142	258	85	0.441	71	135	44	0.446	54	99	24	0.415
rs207906	*XRCC5*	G/A	464	127	12	603	0.125	466	127	9	602	0.12	83	33	1	0.150	383	94	8	0.113	198	48	3	0.108	140	34	4	0.118
rs2228000	*XPC*	C/T	267	277	59	603	0.328	314	235	54	603	0.284	59	48	10	0.291	255	187	44	0.283	134	94	22	0.276	91	72	15	0.287
rs2228001	*XPC*	A/C	220	284	94	598	0.395	207	231	92	530	0.392	42	43	22	0.407	165	188	70	0.388	82	97	38	0.399	58	70	26	0.396
rs2228006	*PMS2*	G/A	436	140	20	596	0.151	371	146	13	530	0.162	69	34	4	0.196	302	112	9	0.154	154	57	7	0.163	108	44	1	0.150
rs2238463	*ERCC4*	C/G	210	303	89	602	0.400	250	275	76	601	0.355	58	44	15	0.316	192	231	61	0.365	93	122	34	0.382	73	84	20	0.350
rs2252775	*RAD50*	A/C	370	213	18	601	0.207	367	214	20	601	0.211	71	42	4	0.214	296	172	16	0.211	147	92	9	0.222	114	59	5	0.194
rs2272615	*POLB*	A/G	459	125	11	595	0.124	464	120	11	595	0.119	92	23	2	0.115	372	97	9	0.120	197	44	6	0.113	128	43	3	0.141
rs2286940	*MLH1*	C/T	170	280	149	599	0.482	154	308	139	601	0.488	31	61	25	0.474	129	247	108	0.478	67	125	57	0.480	47	92	38	0.475
rs2303428	*MSH2*	T/C	495	98	9	602	0.095	476	120	6	602	0.110	84	32	1	0.145	392	88	5	0.101	204	41	4	0.098	138	39	1	0.115
rs2308321	*MGMT*	A/G	476	90	11	577	0.097	468	97	2	567	0.089	88	18	—	0.085	380	79	2	0.090	193	40	—	0.085	136	33	1	0.103
rs2345060	*PMS2*	A/G	334	229	38	601	0.254	365	206	31	602	0.223	74	37	6	0.209	291	169	25	0.226	151	84	15	0.228	103	66	8	0.232
rs2348244	*MSH6*	T/C	448	144	11	603	0.138	471	127	4	602	0.112	84	32	1	0.145	387	95	3	0.104	202	46	2	0.100	136	40	1	0.119
rs238406	*ERCC2*	G/T	162	282	159	603	0.498	169	268	166	603	0.498	31	55	31	0.500	138	213	135	0.497	69	116	65	0.492	53	76	49	0.489
rs2434470	*ALKBH3*	C/G	349	217	35	601	0.239	370	200	27	597	0.213	67	41	8	0.246	303	159	19	0.205	152	88	9	0.213	107	57	10	0.221
rs2440	*XRCC5*	C/T	185	301	116	602	0.443	177	307	117	601	0.450	38	56	23	0.436	139	251	94	0.454	70	136	42	0.444	51	87	40	0.469
rs25487	*XRCC1*	G/A	230	271	102	603	0.394	254	260	89	603	0.363	53	47	17	0.346	201	213	72	0.367	106	104	40	0.368	72	78	28	0.376
rs26279	*MSH3*	A/G	287	243	70	600	0.319	281	254	68	603	0.323	61	47	9	0.278	220	207	59	0.334	112	104	34	0.344	84	77	17	0.312
rs26779	*MSH3*	G/A	203	301	95	599	0.410	239	276	87	602	0.374	40	63	14	0.389	199	213	73	0.370	103	112	34	0.361	74	71	33	0.385
rs293794	*OGG1*	T/C	410	168	19	597	0.173	401	190	10	601	0.175	76	40	1	0.179	325	150	9	0.174	178	68	4	0.152	110	62	4	0.199
rs3136038	*ERCC4*	C/T	222	298	81	601	0.383	258	277	66	601	0.340	58	44	14	0.310	200	233	52	0.347	98	123	28	0.359	75	84	19	0.343
rs3136228	*MSH6*	T/G	256	274	68	598	0.343	242	280	77	599	0.362	50	51	16	0.355	192	229	61	0.364	98	114	36	0.375	73	84	20	0.350
rs3212948	*ERCC1*	C/G	250	262	89	601	0.366	243	268	85	596	0.367	50	55	12	0.338	193	213	73	0.375	99	112	36	0.372	72	73	30	0.380
rs3212961	*ERCC1*	C/A	468	128	6	602	0.116	466	125	12	603	0.124	88	26	3	0.137	378	99	9	0.120	190	54	6	0.132	138	37	3	0.121
rs3212986	*ERCC1*	G/T	329	223	43	595	0.260	294	200	37	531	0.258	65	37	5	0.220	229	163	32	0.268	122	84	12	0.248	80	59	15	0.289
rs3213245	*XRCC1*	T/C	230	281	90	601	0.384	227	265	110	602	0.403	48	43	26	0.406	179	222	84	0.402	93	110	46	0.406	70	78	30	0.388
rs3218536	*XRCC2*	G/A	486	113	3	602	0.099	483	115	5	603	0.104	100	15	2	0.080	383	100	3	0.109	193	56	1	0.116	142	34	2	0.107
rs3219489	*MUTYH*	G/C	309	248	43	600	0.278	318	242	32	592	0.258	67	40	8	0.243	251	202	24	0.262	124	104	15	0.276	92	76	8	0.261
rs3626	*PCNA*	G/C	455	135	12	602	0.132	460	136	7	603	0.124	88	29	—	0.124	372	107	7	0.124	193	55	2	0.118	135	40	3	0.129
rs3730668	*POLI*	G/T	186	314	98	598	0.426	199	288	107	594	0.423	36	49	29	0.469	163	239	78	0.411	84	115	46	0.422	60	92	25	0.401
rs3793784	*ERCC6*	C/G	200	282	117	599	0.431	211	288	101	600	0.408	45	48	24	0.410	166	240	77	0.408	95	105	48	0.405	57	96	24	0.407
rs4150416	*ERCC3*	T/G	269	273	59	601	0.325	301	255	47	603	0.289	51	61	5	0.303	250	194	42	0.286	132	94	24	0.284	86	79	13	0.295
rs4150441	*ERCC3*	A/G	216	292	92	600	0.397	201	300	98	599	0.414	42	58	17	0.393	159	242	81	0.419	86	116	45	0.417	58	93	27	0.413

rs4150474	*ERCC3*	T/G	325	242	33	600	0.257	353	220	30	603	0.232	65	49	3	0.235	288	171	27	0.231	149	87	14	0.230	104	65	9	0.233
rs4234259	*MLH1*	A/G	165	278	154	597	0.491	150	309	141	600	0.493	31	63	23	0.466	127	246	110	0.482	65	124	59	0.488	47	92	38	0.475
rs4253160	*ERCC6*	A/T	181	290	131	602	0.458	192	293	114	599	0.435	37	54	25	0.448	155	239	89	0.432	87	107	54	0.433	54	94	29	0.429
rs4968451	*BRIP1*	A/C	407	176	17	600	0.175	422	166	13	601	0.160	82	33	2	0.158	340	133	11	0.160	172	71	5	0.163	121	53	4	0.171
rs4986764	*BRIP1*	C/T	224	270	107	601	0.403	232	297	69	598	0.364	35	67	13	0.404	197	230	56	0.354	93	130	25	0.363	76	74	27	0.362
rs4987876	*ATM*	G/T	497	94	9	600	0.093	511	79	11	601	0.084	96	20	1	0.094	415	59	10	0.082	217	26	7	0.080	151	23	2	0.077
rs569143	*MRE11A*	C/G	158	297	146	601	0.490	158	308	132	598	0.478	29	59	28	0.496	130	249	103	0.472	66	127	54	0.476	51	89	37	0.460
rs5744934	*POLE*	A/G	415	168	16	599	0.167	417	159	25	601	0.174	84	29	3	0.151	333	130	22	0.179	174	63	13	0.178	115	54	8	0.198
rs601341	*MRE11A*	G/A	179	307	113	599	0.445	203	299	97	599	0.412	35	63	19	0.432	168	236	78	0.407	84	122	40	0.411	61	88	29	0.410
rs6413436	*RAD52*	T/C	274	263	64	601	0.325	257	261	84	602	0.356	49	50	18	0.368	208	211	66	0.354	108	106	35	0.353	68	85	25	0.379
rs664143	*ATM*	C/T	226	288	89	603	0.386	248	280	73	601	0.354	52	50	15	0.342	196	230	58	0.357	105	116	28	0.345	69	83	25	0.376
rs7182283	*NEIL1*	G/T	171	280	144	595	0.477	169	309	118	596	0.457	29	65	22	0.470	140	244	96	0.454	70	126	49	0.457	55	86	36	0.446
rs735943	*EXO1*	C/T	174	279	149	602	0.479	173	302	124	599	0.459	35	58	24	0.453	138	244	100	0.461	75	130	44	0.438	44	87	44	0.500
rs7797466	*PMS2*	G/A	439	142	20	601	0.151	419	170	13	602	0.163	87	26	4	0.145	332	144	9	0.167	175	69	5	0.159	123	52	3	0.163
rs799917	*BRCA1*	C/T	250	281	69	600	0.349	234	297	69	600	0.363	41	63	13	0.380	193	234	56	0.358	100	118	31	0.361	73	88	15	0.335
rs8305	*POLI*	A/G	329	236	38	603	0.259	308	245	50	603	0.286	66	43	8	0.252	242	202	42	0.294	130	99	21	0.282	85	77	16	0.306
rs861528	*XRCC3*	G/A	350	205	33	588	0.230	279	219	30	528	0.264	61	43	3	0.229	218	176	27	0.273	124	81	12	0.242	66	73	13	0.326
rs861531	*XRCC3*	G/T	230	277	88	595	0.381	210	298	89	597	0.399	43	56	17	0.388	167	242	72	0.401	97	116	33	0.370	50	96	31	0.446
rs861539	*XRCC3*	C/T	238	277	88	603	0.376	227	293	83	603	0.381	43	58	16	0.385	184	235	67	0.380	106	115	29	0.346	57	91	30	0.424
rs9350	*EXO1*	C/T	430	150	19	599	0.157	439	143	14	596	0.143	87	25	4	0.142	352	118	10	0.144	184	58	4	0.134	127	45	4	0.151
rs963248	*XRCC4*	A/G	422	165	15	602	0.162	419	168	16	603	0.166	83	33	1	0.150	336	135	15	0.170	164	77	9	0.190	127	48	3	0.152
rs9876116	*MLH1*	A/G	173	279	149	601	0.480	161	308	131	600	0.475	29	64	24	0.479	137	244	102	0.464	70	120	58	0.476	52	93	32	0.444
rs9894946	*TP53*	G/A	409	165	18	592	0.170	452	138	6	596	0.126	92	23	—	0.100	360	115	6	0.132	188	56	4	0.129	123	51	2	0.156

n, number of individuals; A/a, major/minor alleles; MAF, minor allele frequency.
N, number of individuals successfully genotyped.

Supplementary Table 3: Significant SNPs in DNA repair genes associated with gastric cancer risk.

		Univariate analysis				Multivariate analysis*			
		Codominant	Dominant	Recessive	Log-additive	Codominant	Dominant	Recessive	Log-Additive
Gen	db SNP ID	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value
TP53	rs1042522	0.82 (0.52–1.31) 0.471	0.68 (0.54–0.85) **0.001**	0.97 (0.61-1.53) 0.912	0.78 (0.64–0.93) **0.007**	0.88 (0.55–1.42) 0.609	0.67 (0.53–0.85) **0.001**	1.05 (0.66–1.67) 0.832	0.78 (0.65–0.94) **0.009**
RAD52	rs11226	1.49 (1.06–2.10) **0.024**	1.24 (0.96–1.59) 0.092	1.37 (1.02–1.86) **0.039**	1.21 (1.03–1.43) **0.023**	1.51 (1.06–2.13) **0.017**	1.23 (0.95–1.59) 0.111	1.40 (1.03–1.91) **0.032**	1.21 (1.02–1.44) **0.025**
ERCC5	rs17655	0.67 (0.42–1.05) 0.085	0.80 (0.64–1.01) 0.058	0.72 (0.46–1.12) 0.144	0.82 (0.69–0.99) **0.035**	0.63 (0.39–1.01) 0.052	0.77 (0.61–0.97) **0.025**	0.69 (0.43–1.09) 0.109	0.79 (0.66–0.96) **0.015**
POLG	rs176641	1.25 (0.86–1.79) 0.265	1.32 (1.05–1.67) **0.016**	1.06 (0.76–1.49) 0.721	1.18 (1.00–1.39) 0.055	1.24 (0.86–1.80) 0.108	1.29 (1.02–1.63) **0.036**	1.08 (0.76–1.53) 0.659	1.16 (0.98–1.38) 0.082
BRCA2	rs1801406	0.58 (0.36–0.92) **0.028**	0.99 (0.79–1.24) 0.913	0.56 (0.36–0.88) **0.011**	0.90 (0.75–1.08) 0.252	0.61 (0.38–0.97) **0.038**	0.98 (0.77–1.23) 0.837	0.60 (0.38–0.95) **0.027**	0.90 (0.75–1.09) 0.277
LIG3	rs2074522	6.67 (1.50–29.67) **0.009**	1.21 (0.89-1.64) 0.227	6.59 (1.48–29.28) **0.002**	1.30 (0.98 –1.71) 0.064	7.15 (1.60–31.97) **0.007**	1.22 (0.89–1.67) 0.217	7.05 (1.58–31.53) **0.001**	1.32 (0.99–1.75) 0.055
XPC	rs2228000	0.78 (0.52–1.17) 0.257	0.73 (0.58–0.92) **0.006**	0.91 (0.62–1.34) 0.621	0.82 (0.68–0.97) **0.021**	0.82 (0.55–1.24) 0.829	0.73 (0.58–0.92) **0.008**	0.96 (0.65–1.43) 0.854	0.83 (0.69–0.99) **0.035**
ERCC4	rs2238463	0.71 (0.50–1.02) 0.070	0.75 (0.60–0.95) **0.016**	0.83 (0.60–1.16) 0.280	0.82 (0.70–0.97) **0.023**	0.71 (0.49–1.03) 0.059	0.75 (0.59–0.95) **0.019**	0.83 (0.59–1.17) 0.325	0.82 (0.69–0.98) **0.025**
MGMT	rs2308321	0.18 (0.04–0.84) **0.028**	1.00 (0.73–1.35) 0.984	0.18 (0.04–0.83) **0.009**	0.91 (0.69–1.20) 0.517	0.20 (0.04–0.93) **0.039**	1.03 (0.75–1.41) 0.858	0.20 (0.04–0.91) **0.015**	0.94 (0.71–1.25) 0.665
MSH3	rs26779	0.77 (0.55–1.10) 0.159	0.78 (0.62–0.98) **0.036**	0.90 (0.62–0.98) 0.496	0.86 (0.73–1.01) 0.068	0.80 (0.56–1.14) 0.242	0.81 (0.64–1.04) 0.093	0.90 (0.65–1.24) 0.509	0.88 (0.74–1.04) 0.127
ERCC4	rs3136038	0.70 (0.48–1.01) 0.073	0.78 (0.62–0.98) **0.033**	0.79 (0.56–1.12) 0.186	0.83 (0.70–0.98) **0.027**	0.68 (0.46–0.99) **0.049**	0.77 (0.61–0.98) **0.032**	0.76 (0.53–1.09) 0.138	0.81 (0.68–0.97) **0.021**
BRIP1	rs4986764	0.62 (0.43–0.88) **0.009**	0.94 (0.74–1.18) 0.586	0.60 (0.43–0.83) **0.002**	0.85 (0.72–0.99) **0.049**	0.62 (0.43–0.89) **0.007**	0.94 (0.74–1.20) 0.633	0.59 (0.42–0.83) **0.002**	0.85 (0.72–1.00) 0.055
XRCC3	rs861528	1.14 (0.67–1.91) 0.690	1.31 (1.04–1.36) **0.024**	1.01 (0.61–1.69) 0.959	1.20 (0.99–1.46) 0.061	1.20 (0.71–2.03) 0.432	1.35 (1.06–1.72) **0.015**	1.05 (0.62–1.76) 0.862	1.23 (1.01–1.51) **0.038**
TP53	rs9894946	0.30 (0.11–0.76) **0.011**	0.71 (0.55–0.92) **0.009**	0.32 (0.13–0.82) **0.010**	0.70 (0.56–0.88) **0.002**	0.21 (0.07–0.64) **0.001**	0.69 (0.53–0.90) **0.006**	0.23 (0.08–0.68) **0.002**	0.67 (0.53–0.85) **0.001**

OR, odds ratio; 95% CI, 95% confidence interval.

ORs and 95% CI in the multivariate analysis were adjusted for age, gender, *H. pylori* infection, smoking habit, and family history of GC.

P values < 0.05 are highlighted in bold.

Supplementary Table 4: Association of DNA repair gene polymorphisms with risk of *Helicobacter pylori* infection in healthy controls.

		***Helicobacter pylori* infection**					**CagA status**					**VacA status**				
		Log-additive genetic model					**Log-additive genetic model**					**Log-additive genetic model**				
		95% CI					**95% CI**					**95% CI**				
db SNP ID	**Gen**	**OR[a]**	**Lower**	**Upper**	***P*-value**	**FDR[b]**	**OR[a]**	**Lower**	**Upper**	***P*-value**	**FDR[b]**	**OR[a]**	**Lower**	**Upper**	***P*-value**	**FDR[b]**
rs10079641	*MSH3*	0.72	0.49	1.05	0.092	0.583	0.88	0.52	1.50	0.651	0.964	0.65	0.39	1.07	**0.025**	0.672
rs1042522	*TP53*	1.16	0.89	1.51	0.277	0.869	0.84	0.58	1.20	0.339	0.924	0.93	0.66	1.33	0.708	0.968
rs1047768	*ERCC5*	1.13	0.90	1.42	0.301	0.869	0.95	0.70	1.29	0.741	0.964	0.81	0.60	1.09	0.170	0.708
rs1047840	*EXO1*	0.95	0.75	1.20	0.654	0.989	0.70	0.51	0.97	**0.033**	0.924	0.99	0.73	1.36	0.963	0.973
rs1048771	*RAD54L*	1.09	0.75	1.59	0.657	0.989	0.66	0.40	1.08	0.102	0.924	0.78	0.48	1.28	0.282	0.794
rs1051677	*XRCC5*	1.15	0.76	1.74	0.517	0.989	0.71	0.41	1.21	0.208	0.924	0.66	0.39	1.11	0.120	0.672
rs1051685	*XRCC5*	1.18	0.81	1.73	0.384	0.869	1.08	0.65	1.78	0.766	0.964	0.92	0.57	1.47	0.719	0.970
rs1052133	*OGG1*	1.16	0.87	1.54	0.321	0.869	0.88	0.61	1.27	0.485	0.940	0.81	0.57	1.15	0.239	0.739
rs1059262	*ALKBH2*	0.86	0.64	1.15	0.301	0.869	0.89	0.59	1.35	0.587	0.940	1.18	0.90	1.54	0.236	0.739
rs1060915	*BRCA1*	1.05	0.82	1.35	0.706	0.989	1.17	0.83	1.64	0.371	0.924	1.02	0.74	1.41	0.903	0.973
rs11226	*RAD52*	1.02	0.80	1.29	0.881	0.989	1	0.72	1.39	0.983	0.990	0.91	0.66	1.25	0.553	0.910
rs1130409	*APEX1*	1	0.79	1.26	0.995	0.995	1.18	0.86	1.62	0.318	0.924	1.16	0.85	1.57	0.356	0.854
rs1136410	*PARP1*	1.20	0.84	1.73	0.316	0.869	1.15	0.71	1.86	0.580	0.940	1.09	0.68	1.72	0.287	0.794
rs13180316	*XRCC4*	0.94	0.72	1.21	0.615	0.989	1.34	0.92	1.96	0.118	0.924	0.8	0.56	1.13	0.198	0.708
rs13181	*ERCC2*	0.93	0.74	1.18	0.570	0.989	0.99	0.71	1.38	0.943	0.964	0.75	0.54	1.03	0.074	0.672
rs1346044	*WRN*	1.29	0.98	1.70	0.072	0.583	0.76	0.53	1.08	0.131	0.924	0.87	0.62	1.23	0.438	0.885
rs144848	*BRCA2*	1.03	0.79	1.34	0.840	0.989	0.85	0.59	1.22	0.380	0.924	0.74	0.52	1.05	0.095	0.672
rs1478485	*XRCC4*	1.12	0.89	1.42	0.330	0.869	0.98	0.71	1.35	0.895	0.964	1.01	0.73	1.38	0.973	0.973
rs1540354	*MLH1*	0.97	0.69	1.36	0.856	0.989	1.54	0.91	2.60	0.097	0.924	0.82	0.52	1.30	0.402	0.885
rs1614984	*TP53*	1.20	0.95	1.53	0.130	0.666	1.09	0.79	1.51	0.592	0.940	1.19	0.87	1.62	0.280	0.794
rs1618536	*ERCC2*	1.21	0.96	1.51	0.101	0.583	0.90	0.67	1.23	0.522	0.940	0.99	0.73	1.33	0.944	0.973
rs1650697	*MSH3*	1.03	0.79	1.34	0.831	0.989	0.95	0.66	1.35	0.762	0.964	1.06	0.75	1.50	0.747	0.973
rs174538	*FEN1*	0.98	0.76	1.26	0.865	0.989	0.95	0.67	1.35	0.771	0.964	1.32	0.93	1.87	0.116	0.672
rs175080	*MLH3*	0.98	0.78	1.23	0.828	0.989	0.88	0.64	1.2	0.423	0.924	1.02	0.76	1.39	0.884	0.973
rs1760944	*APEX1*	0.88	0.68	1.13	0.315	0.869	0.96	0.68	1.34	0.804	0.964	0.78	0.56	1.08	0.131	0.672
rs17655	*ERCC5*	1.13	0.87	1.46	0.360	0.869	1.23	0.86	1.74	0.253	0.924	0.82	0.59	1.14	0.239	0.739
rs176641	*POLG*	1.06	0.83	1.35	0.634	0.989	0.86	0.62	1.20	0.382	0.924	1.14	0.83	1.57	0.421	0.885
rs1776148	*EXO1*	1.05	0.83	1.32	0.713	0.989	0.90	0.65	1.24	0.512	0.940	0.94	0.69	1.28	0.693	0.968
rs1799793	*ERCC2*	0.94	0.73	1.20	0.603	0.989	1.01	0.72	1.42	0.946	0.964	0.85	0.62	1.18	0.328	0.805
rs1799794	*XRCC3*	0.95	0.73	1.24	0.725	0.989	1.16	0.80	1.68	0.426	0.924	1.12	0.78	1.59	0.544	0.910
rs1799796	*XRCC3*	0.80	0.61	1.05	0.108	0.583	1.21	0.81	1.81	0.352	0.924	1.10	0.75	1.61	0.635	0.939
rs1799801	*ERCC4*	0.99	0.77	1.27	0.933	0.989	0.94	0.68	1.31	0.723	0.964	1.28	0.92	1.78	0.137	0.672
rs1799955	*BRCA2*	0.73	0.55	0.97	**0.030**	0.539	0.98	0.65	1.46	0.907	0.964	1.23	0.82	1.83	0.316	0.798
rs1799966	*BRCA1*	1.05	0.82	1.34	0.712	0.989	1.12	0.80	1.56	0.526	0.940	0.99	0.71	1.36	0.932	0.973
rs1799977	*MLH1*	0.96	0.75	1.22	0.725	0.989	0.79	0.57	1.09	0.158	0.924	0.82	0.60	1.12	0.203	0.708
rs1800067	*ERCC4*	1.31	0.91	1.91	0.146	0.685	0.89	0.56	1.41	0.613	0.945	1.37	0.85	2.21	0.189	0.708
rs1800389	*WRN*	1.01	0.78	1.30	0.947	0.989	0.96	0.68	1.35	0.808	0.964	1.17	0.83	1.64	0.370	0.867
rs1800734	*MLH1*	0.92	0.70	1.19	0.522	0.989	1.21	0.83	1.76	0.319	0.924	1.21	0.85	1.74	0.289	0.794
rs1800935	*MSH6*	1.13	0.87	1.48	0.348	0.869	0.92	0.65	1.31	0.655	0.964	0.75	0.53	1.05	0.099	0.672
rs1800975	*XPA*	1.06	0.83	1.36	0.618	0.989	1.10	0.79	1.54	0.579	0.940	0.87	0.63	1.19	0.386	0.885

rs1801406	*BRCA2*	0.77	0.60	1	**0.048**	0.583	0.97	0.68	1.39	0.874	0.964	1.04	0.74	1.47	0.830	0.973
rs1801516	*ATM*	1	0.71	1.41	0.985	0.994	1.62	0.98	2.67	0.153	0.924	1.77	1.09	2.87	**0.017**	0.614
rs1802904	*ATR*	1.25	0.86	1.80	0.235	0.869	1.24	0.76	2.02	0.383	0.924	0.99	0.63	1.56	0.971	0.973
rs1805386	*LIG4*	1.30	0.95	1.80	0.102	0.583	1.18	0.77	1.79	0.441	0.924	0.96	0.76	1.22	0.751	0.973
rs1805388	*LIG4*	0.99	0.70	1.39	0.937	0.989	1.26	0.77	2.05	0.357	0.924	0.84	0.54	1.32	0.451	0.885
rs1805794	*NBS1*	1.11	0.87	1.43	0.394	0.869	1.02	0.73	1.44	0.892	0.964	1.01	0.73	1.40	0.945	0.973
rs1981928	*MSH2*	0.87	0.67	1.13	0.295	0.869	0.87	0.62	1.24	0.444	0.924	0.77	0.55	1.08	0.128	0.672
rs2020911	*MSH6*	0.92	0.72	1.16	0.482	0.989	0.83	0.6	1.15	0.265	0.924	0.94	0.68	1.28	0.678	0.963
rs2040639	*XRCC2*	1.06	0.84	1.33	0.614	0.989	0.94	0.69	1.28	0.696	0.964	0.97	0.72	1.31	0.845	0.973
rs2048718	*BRIP1*	1.16	0.92	1.48	0.213	0.869	0.69	0.49	0.95	**0.023**	0.924	0.73	0.53	1.01	0.054	0.672
rs20580	*LIG1*	1.34	1.07	1.69	**0.011**	0.420	1.01	0.74	1.39	0.940	0.964	1.26	0.92	1.71	0.147	0.687
rs2074522	*LIG3*	1.10	0.71	1.72	0.752	0.989	1.30	0.70	2.40	0.825	0.964	1.22	0.68	2.19	0.494	0.909
rs2075685	*XRCC4*	1.22	0.97	1.55	0.090	0.583	0.92	0.67	1.26	0.584	0.940	1.13	0.83	1.54	0.426	0.885
rs207906	*XRCC5*	1.03	0.73	1.45	0.882	0.989	1.27	0.78	2.08	0.327	0.924	1.06	0.67	1.67	0.799	0.973
rs2228000	*XPC*	0.78	0.60	1	**0.048**	0.583	1.07	0.75	1.51	0.721	0.964	0.91	0.65	1.27	0.583	0.925
rs2228001	*XPC*	1.03	0.81	1.30	0.823	0.989	1.22	0.88	1.69	0.226	0.924	1.03	0.76	1.41	0.837	0.973
rs2228006	*PMS2*	1.04	0.76	1.42	0.802	0.989	1.25	0.81	1.94	0.307	0.924	1.06	0.70	1.59	0.787	0.973
rs2238463	*ERCC4*	1.05	0.82	1.34	0.696	0.989	1.02	0.73	1.42	0.912	0.964	1.36	0.99	1.89	0.059	0.672
rs2252775	*RAD50*	0.88	0.66	1.19	0.414	0.885	0.93	0.62	1.39	0.733	0.964	1.14	0.77	1.70	0.505	0.909
rs2272615	*POLB*	1.03	0.73	1.47	0.851	0.989	1.23	0.76	2.01	0.395	0.924	1.27	0.79	2.04	0.318	0.798
rs2286940	*MLH1*	1.01	0.81	1.26	0.940	0.989	0.83	0.61	1.13	0.233	0.924	0.89	0.66	1.19	0.436	0.885
rs2303428	*MSH2*	0.96	0.66	1.40	0.826	0.989	0.72	0.44	1.18	0.199	0.924	0.88	0.54	1.45	0.626	0.939
rs2308321	*MGMT*	0.89	0.66	1.21	0.463	0.885	1.30	0.72	2.35	0.369	0.924	0.84	0.50	1.43	0.530	0.909
rs2345060	*PMS2*	1.22	0.93	1.6	0.141	0.685	0.89	0.62	1.28	0.535	0.940	1.11	0.78	1.58	0.565	0.910
rs2348244	*MSH6*	0.91	0.65	1.27	0.584	0.989	1.16	0.72	1.86	0.541	0.940	1.54	0.95	2.48	0.069	0.672
rs238406	*ERCC2*	1.21	0.97	1.52	0.091	0.583	0.87	0.64	1.17	0.355	0.924	0.94	0.70	1.27	0.704	0.968
rs2434470	*ALKBH3*	0.94	0.72	1.23	0.645	0.989	1.40	0.95	2.06	0.086	0.924	0.95	0.67	1.36	0.782	0.973
rs2440	*XRCC5*	0.95	0.76	1.21	0.695	0.989	1.03	0.75	1.42	0.837	0.964	1.08	0.80	1.47	0.607	0.939
rs25487	*XRCC1*	1.11	0.88	1.39	0.394	0.869	1.13	0.82	1.55	0.454	0.924	0.74	0.55	1.01	0.054	0.672
rs26279	*MSH3*	1.02	0.80	1.30	0.875	0.989	1.20	0.86	1.67	0.292	0.924	1.01	0.74	1.39	0.933	0.973
rs26779	*MSH3*	0.88	0.69	1.12	0.285	0.869	0.93	0.67	1.30	0.676	0.964	0.98	0.71	1.34	0.876	0.973
rs293794	*OGG1*	0.87	0.65	1.18	0.388	0.869	1.22	0.79	1.87	0.363	0.924	1.01	0.68	1.51	0.967	0.973
rs3136038	*ERCC4*	1.07	0.84	1.36	0.604	0.989	1.04	0.74	1.44	0.835	0.964	1.37	0.99	1.90	0.056	0.672
rs3136228	*MSH6*	1.09	0.85	1.39	0.515	0.989	0.96	0.69	1.35	0.824	0.964	0.74	0.53	1.02	0.067	0.672
rs3212948	*ERCC1*	0.80	0.63	1.01	0.061	0.583	0.91	0.66	1.25	0.555	0.940	0.85	0.62	1.16	0.294	0.794
rs3212961	*ERCC1*	0.80	0.56	1.15	0.232	0.869	1.15	0.67	1.96	0.946	0.964	1.33	0.78	2.26	0.518	0.909
rs3212986	*ERCC1*	0.89	0.69	1.16	0.391	0.869	0.87	0.61	1.26	0.472	0.940	0.76	0.54	1.08	0.133	0.672
rs3213245	*XRCC1*	1	0.79	1.27	0.969	0.989	0.94	0.68	1.28	0.685	0.964	1.21	0.89	1.64	0.226	0.739
rs3218536	*XRCC2*	1.01	0.68	1.50	0.961	0.989	1.18	0.67	2.07	0.843	0.964	1.36	0.78	2.36	0.610	0.939
rs3219489	*MUTYH*	0.99	0.76	1.29	0.945	0.989	0.95	0.66	1.37	0.801	0.964	1.03	0.73	1.47	0.863	0.973
rs3626	*PCNA*	0.91	0.65	1.28	0.590	0.989	1.61	0.95	2.71	0.150	0.924	1.37	0.85	2.22	0.193	0.708
rs3730668	*POLI*	1.08	0.85	1.38	0.524	0.989	1.42	1	2.01	**0.047**	0.924	1.14	0.82	1.59	0.446	0.885
rs3793784	*ERCC6*	1.22	0.96	1.53	0.097	0.583	0.85	0.62	1.17	0.330	0.924	0.99	0.73	1.34	0.934	0.973
rs4150416	*ERCC3*	1.26	0.98	1.62	0.075	0.583	1.08	0.76	1.52	0.670	0.964	0.79	0.57	1.09	0.153	0.687
rs4150441	*ERCC3*	0.98	0.77	1.25	0.885	0.989	1.02	0.75	1.40	0.884	0.964	1.14	0.84	1.55	0.406	0.885
rs4150474	*ERCC3*	1.18	0.9	1.54	0.236	0.869	1.02	0.71	1.47	0.899	0.964	0.79	0.56	1.12	0.194	0.708

rs4234259	*MLH1*	1	0.80	1.25	0.970	0.989	0.84	0.62	1.14	0.269	0.924	0.91	0.68	1.21	0.506	0.909
rs4253160	*ERCC6*	1.23	0.98	1.55	0.077	0.583	0.87	0.63	1.19	0.369	0.924	1.02	0.75	1.38	0.902	0.973
rs4968451	*BRIP1*	1.36	0.99	1.87	0.052	0.583	0.77	0.52	1.14	0.194	0.924	0.92	0.62	1.35	0.658	0.961
rs4986764	*BRIP1*	1.01	0.81	1.27	0.920	0.989	1.16	0.84	1.59	0.365	0.924	0.97	0.71	1.31	0.826	0.973
rs4987876	*ATM*	1.52	1.01	2.28	**0.041**	0.583	0.83	0.51	1.33	0.436	0.924	0.96	0.60	1.54	0.864	0.973
rs569143	*MRE11A*	0.98	0.78	1.23	0.835	0.989	1.09	0.79	1.49	0.601	0.941	0.91	0.67	1.23	0.523	0.909
rs5744934	*POLE*	1.17	0.85	1.61	0.327	0.869	1	0.66	1.52	0.990	0.990	0.94	0.63	1.41	0.765	0.973
rs601341	*MRE11A*	0.89	0.70	1.13	0.326	0.869	0.98	0.71	1.36	0.905	0.964	1.12	0.81	1.53	0.491	0.909
rs6413436	*RAD52*	1.08	0.84	1.38	0.543	0.989	0.86	0.61	1.2	0.363	0.924	0.95	0.69	1.32	0.780	0.973
rs664143	*ATM*	1	0.78	1.26	0.971	0.989	0.96	0.69	1.34	0.825	0.964	0.95	0.69	1.31	0.750	0.973
rs7182283	*NEIL1*	0.89	0.71	1.12	0.313	0.869	0.76	0.56	1.04	0.090	0.924	0.85	0.63	1.16	0.308	0.798
rs735943	*EXO1*	1.11	0.89	1.39	0.358	0.869	0.89	0.65	1.20	0.429	0.924	1.29	0.96	1.74	0.085	0.672
rs7797466	*PMS2*	0.78	0.57	1.06	0.107	0.583	1.14	0.72	1.81	0.566	0.940	1.04	0.68	1.61	0.844	0.973
rs799917	*BRCA1*	1.04	0.81	1.33	0.782	0.989	1.07	0.76	1.49	0.708	0.964	0.93	0.68	1.29	0.676	0.963
rs8305	*POLI*	1.03	0.79	1.35	0.821	0.989	0.87	0.61	1.25	0.453	0.924	1.31	0.92	1.89	0.134	0.672
rs861528	*XRCC3*	1.12	0.85	1.48	0.418	0.885	0.90	0.62	1.30	0.580	0.940	0.88	0.62	1.26	0.491	0.909
rs861531	*XRCC3*	1.15	0.91	1.47	0.240	0.869	0.81	0.59	1.11	0.181	0.924	0.81	0.60	1.10	0.186	0.708
rs861539	*XRCC3*	1.12	0.88	1.41	0.363	0.869	0.79	0.57	1.08	0.135	0.924	0.83	0.61	1.12	0.217	0.731
rs9350	*EXO1*	0.83	0.61	1.13	0.250	0.869	0.73	0.48	1.12	0.155	0.924	0.72	0.48	1.10	0.131	0.672
rs963248	*XRCC4*	0.96	0.70	1.31	0.799	0.989	0.97	0.63	1.51	0.906	0.964	0.88	0.58	1.34	0.557	0.910
rs9876116	*MLH1*	0.99	0.79	1.24	0.954	0.989	0.80	0.59	1.08	0.139	0.924	0.93	0.70	1.25	0.629	0.939
rs9894946	*TP53*	0.96	0.71	1.31	0.807	0.989	0.83	0.55	1.25	0.379	0.924	1.02	0.68	1.54	0.906	0.973

OR, odds ratio; CI, confidence interval.

[a]ORs adjusted by gender, age, smoking habit, and family history of GC.

[b]QFDR-values obtained after applying the False Discovery Rate (FDR) test.

P-values <0.05 are highlighted in bold.

Supplementary Table 5: Significant SNPs associated with gastric cancer risk. Association analysis stratified by anatomical location of the tumor.

CARDIA GC		Univariate analysis								Multivariate analysis*							
		Codominant		Dominant		Recessive		Log-additive		Codominant		Dominant		Recessive		Log-Additive	
Gen	**db SNP ID**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**
RAD52	rs11226	1.81 (0.99-3.30)	0.112	1.58 (0.99-2.58)	0.059	1.40 (0.84-2.34)	0.202	1.35 (1.01-1.82)	**0.042**	1.65 (0.88-3.09)	0.143	1.59 (0.99-2.57)	**0.049**	1.25 (0.73-2.14)	0.416	1.31 (0.97-1.77)	0.081
ERCC4	rs1799801	0.74 (0.37-1.47)	0.508	0.57 (0.38-0.85)	**0.005**	0.95 (0.48-1.87)	0.855	0.70 (0.51-0.97)	**0.027**	0.66 (0.31-1.42)	0.289	0.58 (0.38-0.88)	**0.010**	0.84 (0.40-1.77)	0.640	0.69 (0.49-0.97)	**0.028**
MLH1	rs1799977	1.64 (0.89-3.01)	0.128	1.52 (1.01-2.30)	**0.042**	1.32 (0.76-2.31)	0.339	1.32 (1.00-1.76)	0.055	1.65 (0.87-3.11)	0.122	1.46 (0.95-2.24)	0.079	1.38 (0.77-2.47)	0.291	1.31 (0.97-1.77)	0.075
LIG4	rs1805388	1.95 (0.52-7.26)	0.399	1.60 (1.03-2.50)	**0.041**	1.72 (0.46-6.35)	0.440	1.52 (1.03-2.24)	**0.041**	2.16 (0.56-8.29)	0.261	1.58 (0.99-2.51)	0.051	1.91 (0.50-7.26)	0.368	1.52 (1.01-2.28)	**0.048**
BRIP1	rs2048718	0.37 (0.17-0.78)	**0.007**	0.72 (0.47-1.10)	0.130	0.40 (0.20-0.82)	**0.005**	0.68 (0.50-0.93)	**0.014**	0.43 (0.20-0.93)	**0.031**	0.71 (0.46-1.11)	0.135	0.49 (0.24-0.93)	**0.034**	0.71 (0.51-0.96)	**0.033**
ERCC4	rs2238463	0.61 (0.33-1.13)	0.145	0.54 (0.37-0.81)	**0.002**	0.85 (0.47-1.52)	0.575	0.69 (0.51-0.95)	**0.017**	0.57 (0.29-1.10)	0.096	0.54 (0.35-0.81)	**0.003**	0.79 (0.42-1.49)	0.462	0.67 (0.49-0.92)	**0.012**
ERCC4	rs3136038	0.66 (0.35-1.25)	0.229	0.59 (0.39-0.87)	**0.008**	0.88 (0.48-1.61)	0.678	0.72 (0.53-0.98)	**0.032**	0.60 (0.30-1.19)	0.143	0.57 (0.38-0.87)	**0.009**	0.80 (0.42-1.53)	0.486	0.69 (0.50-0.96)	**0.023**
POL1	rs3730668	1.53 (0.88-2.64)	0.152	0.98 (0.64-1.51)	0.920	1.74 (1.08-2.80)	**0.025**	1.20 (0.90-1.60)	0.222	1.49 (0.84-2.63)	0.175	0.98 (0.63-1.54)	0.938	1.68 (1.02-2.74)	**0.046**	1.19 (0.88-1.60)	0.268
TP53	rs9894946	NA		0.56 (0.34-0.91)	**0.015**	NA		0.54 (0.34-0.86)	**0.020**	NA		0.51 (0.30-0.86)	**0.011**	NA		0.50 (0.30-0.81)	**0.002**
NON-CARDIA GC		**Univariate analysis**								**Multivariate analysis***							
		Codominant		**Dominant**		**Recessive**		**Log-additive**		**Codominant**		**Dominant**		**Recessive**		**Log-Additive**	
Gen	**db SNP ID**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**
TP53	rs1042522	0.91 (0.56-1.47)	0.715	0.67 (0.52-0.85)	**0.001**	1.09 (0.68-1.74)	0.724	0.78 (0.64-0.95)	**0.013**	1.01 (0.62-1.66)	0.938	0.67 (0.52-0.87)	**0.001**	1.22 (0.76-1.97)	0.416	0.80 (0.65-0.98)	**0.028**
POLG	rs176641	1.27 (0.86-1.88)	0.232	1.42 (1.11-1.82)	**0.004**	1.03 (0.72-1.48)	0.864	1.21 (1.02-1.45)	**0.032**	1.27 (0.85-1.89)	0.245	1.40 (1.09-1.81)	**0.008**	1.04 (0.72-1.50)	0.848	1.21 (1.00-1.46)	0.054
BRCA2	rs1801406	0.56 (0.34-0.92)	**0.021**	0.96 (0.75-1.22)	0.734	0.55 (0.33-0.89)	**0.012**	0.88 (0.72-1.07)	0.191	0.58 (0.35-0.97)	**0.039**	0.96 (0.75-1.23)	0.761	0.57 (0.34-0.94)	**0.023**	0.89 (0.73-1.08)	0.235
LIG3	rs2074522	7.7 (1.73-34.90)	**0.002**	1.32 (0.961.82)	0.083	7.57 (1.69-34.97)	**0.001**	1.42 (1.06-1.89)	**0.017**	8.20 (1.81-37.14)	**0.006**	1.37 (0.99-1.90)	0.057	7.94 (1.76-35.91)	**0.001**	1.46 (1.09-1.96)	**0.010**
XPC	rs2228000	0.78 (0.51-1.20)	0.281	0.72 (0.57-0.91)	**0.007**	0.92 (0.61-1.38)	0.681	0.81 (0.67-0.97)	**0.024**	0.81 (0.53-1.26)	0.354	0.70 (0.55-0.90)	**0.004**	0.98 (0.64-1.48)	0.907	0.81 (0.67-0.98)	**0.026**
MSH6	rs2348244	0.32 (0.09-1.14)	0.101	0.73 (0.55-0.98)	**0.032**	0.33 (0.09-1.21)	0.068	0.72 (0.55-0.94)	**0.016**	0.33 (0.09-1.20)	0.092	0.74 (0.55-0.99)	**0.044**	0.35 (0.10-1.27)	0.082	0.73 (0.56-0.96)	**0.023**
MSH3	rs26779	0.78 (0.55-1.13)	0.198	0.74 (0.58-0.94)	**0.015**	0.94 (0.67-1.31)	0.714	0.85 (0.71-1.01)	0.059	0.80 (0.55-1.17)	0.259	0.76 (0.59-0.99)	**0.039**	0.94 (0.67-1.33)	0.745	0.86 (0.72-1.03)	0.106
ERCC3	rs4150416	0.77 (0.50-1.18)	0.232	0.76 (0.60-0.97)	**0.028**	0.87 (0.57-1.32)	0.506	0.83 (0.69-0.99)	**0.047**	0.72 (0.46-1.13)	0.157	0.73 (0.57-0.94)	**0.013**	0.84 (0.55-1.29)	0.429	0.80 (0.66-0.97)	**0.024**
BRIP1	rs4986764	0.60 (0.41-0.87)	**0.007**	0.86 (0.67-1.10)	0.238	0.61 (0.43-0.86)	**0.004**	0.82 (0.69-0.97)	**0.021**	0.58 (0.39-0.86)	**0.007**	0.87 (0.67-1.11)	0.249	0.59 (0.41-0.85)	**0.003**	0.81 (0.68- 0.97)	**0.022**
XRCC3	rs861528	1.31 (0.77-2.25)	0.332	1.37 (1.06-1.76)	**0.014**	1.15 (0.68-1.95)	0.596	1.26 (1.03-1.55)	**0.027**	1.41 (0.82-2.44)	0.218	1.45 (1.11-1.88)	**0.010**	1.21 (0.71-2.06)	0.494	1.31 (1.06-1.62)	**0.011**
TP53	rs9894946	0.38 (0.15-0.96)	**0.038**	0.75 (0.57-0.98)	**0.036**	0.40 (0.16-1.02)	0.060	0.74 (0.58-0.94)	**0.014**	0.27 (0.09-0.82)	**0.021**	0.74 (0.56-0.98)	**0.033**	0.29 (0.10-0.87)	**0.014**	0.72 (0.56-0.93)	**0.009**

OR, odds ratio; 95% CI, 95% confidence interval; NA, not applied.

ORs and 95% CI in the multivariate analysis were adjusted for age, gender, *H. pylori* infection, smoking habit, and family history of GC.

P values < 0.05 are highlighted in bold.

Supplementary Table 6: Significant SNPs associated with gastric cancer risk. Association analysis stratified by histological tumor type.

INTESTINAL GC		Univariate analysis				Multivariate analysis*			
		Codominant	Dominant	Recessive	Log-additive	Codominant	Dominant	Recessive	Log-Additive
Gen	db SNP ID	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value
TP53	rs1042522	1.05 (0.59-1.85) 0.884	0.73 (0.54-0.98) **0.038**	0.82 (0.47-1.43) 0.466	0.85 (0.66-1.08) 0.170	1.08 (0.60-1.95) 0.793	0.72 (0.53-0.98) **0.037**	0.89 (0.71-2.26) 0.431	0.84 (0.66-1.08) 0.180
ERCC5	rs17655	0.74 (0.42-1.32) 0.332	0.65 (0.48-0.88) **0.005**	0.88 (0.50-1.55) 0.657	0.75 (0.59-0.95) **0.017**	0.62 (0.33-1.16) 0.136	0.60 (0.43-0.82) **0.001**	0.75 (0.40-1.39) 0.351	0.69 (0.53-0.89) **0.003**
POLG	rs176641	1.23 (0.76-2.00) 0.448	1.41 (1.04-1.91) **0.027**	1.00 (0.64-1.57) 0.996	1.19 (0.96-1.49) 0.110	1.25 (0.75-2.06) 0.385	1.40 (1.02-1.93) **0.035**	1.02 (0.64-1.62) 0.936	1.20 (0.96-1.50) 0.117
LIG3	rs2074522	6.15 (1.1-31.94) **0.025**	1.16 (0.78-1.73) 0.461	6.10 (1.1-31.66) **0.021**	1.26 (0.88-1.81) 0.217	6.08 (1.1-32.23) **0.032**	1.21 (0.80-1.82) 0.371	6.0 (1.14-31.53) 0.023	1.30 (0.90-1.89) 0.168
XPC	rs2228000	0.74 (0.44-1.26) 0.299	0.69 (0.51-0.92) **0.013**	0.89 (0.53-1.49) 0.653	0.78 (0.62-0.98) **0.034**	0.78 (0.45-1.35) 0.374	0.69 (0.51-0.94) **0.017**	0.94 (0.55-1.59) 0.808	0.79 (0.62-1.01) 0.052
MSH6	rs2348244	0.40 (0.09-1.84) 0.363	0.69 (0.48-0.99) **0.039**	0.43 (0.10-1.97) 0.237	0.69 (0.50-0.97) **0.029**	0.43 (0.09-2.00) 0.284	0.74 (0.51-1.07) 0.106	0.46 (0.10-2.12) 0.279	0.74 (0.53-1.04) 0.080
ERCC3	rs4150416	0.83 (0.49-1.39) 0.520	0.72 (0.54-0.97) **0.032**	0.98 (0.59-1.61) 0.922	0.82 (0.65-1.03) 0.092	0.77 (0.45-1.32) 0.343	0.68 (0.50-0.92) **0.013**	0.94 (0.56-1.57) 0.815	0.79 (0.62-1.00) 0.053
BRIP1	rs4986764	0.56 (0.34-0.93) **0.025**	0.99 (0.73-1.34) 0.950	0.52 (0.33-0.82) **0.003**	0.85 (0.68-1.05) 0.127	0.53 (0.30-0.87) **0.013**	0.95 (0.69-1.31) 0.751	0.48 (0.29-0.78) **0.001**	0.82 (0.65-1.02) 0.074
EXO1	rs735943	0.69 (0.44-1.05) 0.104	0.94 (0.68-1.30) 0.723	0.65 (0.45-0.95) **0.022**	0.85 (0.69-1.05) 0.124	0.68 (0.44-1.07) 0.097	0.93 (0.66-1.30) 0.672	0.66 (0.45-0.97) **0.032**	0.85 (0.68-1.05) 0.133
TP53	rs9894946	0.48 (0.16-1.45) 0.242	0.71 (0.51-1.00) **0.047**	0.52 (0.181.56) 0.216	0.73 (0.54-0.98) **0.034**	0.37 (0.11-1.29) 0.119	0.71 (0.50-1.02) 0.057	0.40 (0.12-1.38) 0.111	0.71 (0.52-0.98) **0.032**

DIFFUSE GC		Univariate analysis				Multivariate analysis*			
		Codominant	Dominant	Recessive	Log-additive	Codominant	Dominant	Recessive	Log-Additive
Gen	db SNP ID	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value	OR (95% CI) *P* value
TP53	rs1042522	0.83 (0.42-1.65) 0.738	0.63 (0.45-0.89) **0.007**	0.92 (0.57-1.47) 0.730	0.74 (0.56-0.98) **0.032**	1.05 (0.52-2.12) 0.881	0.64 (0.44-0.92) **0.015**	1.01 (0.52-1.98) 0.967	0.77 (0.57-1.05) 0.092
RAD52	rs11226	1.73 (1.03-2.89) **0.041**	1.49 (1.01-2.21) **0.041**	1.40 (0.90-2.18) 0.145	1.32 (1.03-1.70) **0.030**	1.72 (0.99-2.98) 0.052	1.36 (0.90-2.05) 0.141	1.51 (0.94-2.44) 0.095	1.30 (0.99-1.71) 0.055
APEX1	rs1130409	0.66 (0.41-1.04) 0.082	0.65 (0.46-0.93) **0.020**	0.85 (0.57-1.28) 0.432	0.79 (0.63-1.00) 0.052	0.57 (0.35-0.95) **0.030**	0.61 (0.41-0.89) **0.011**	0.76 (0.49-1.19) 0.222	0.74 (0.58-0.96) **0.019**
POLG	rs176641	0.96 (0.53-1.74) 1.00	1.44 (1.02-2.04) **0.038**	0.74 (0.43-1.30) 0.283	1.14 (0.89-1.46) 0.314	0.96 (0.51-1.81) 0.891	1.41 (0.97-2.04) 0.069	0.75 (0.42-1.37) 0.342	1.13 (0.86-1.47) 0.374
XRCC3	rs1799794	0.32 (0.11-0.91) **0.023**	0.95 (0.68-1.33) 0.679	0.31 (0.11-0.88) **0.010**	0.85 (0.64-1.13) 0.248	0.34 (0.12-0.99) **0.047**	0.88 (0.61-1.26) 0.481	0.34 (0.12-0.98) **0.023**	0.81 (0.59-1.09) 0.163
XRCC3	rs861528	2.09 (1.04-4.18) **0.040**	1.92 (1.34-2.75) **0.0003**	1.57 (0.81-3.07) 0.197	1.62 (1.23-2.14) **0.0007**	2.45 (1.18-5.07) **0.016**	2.11 (1.43-3.12) **0.0001**	1.75 (0.87-3.51) 0.128	1.75 (1.30-2.37) **0.0002**
XRCC3	rs861531	1.62 (0.97-2.70) 0.076	1.60 (1.11-2.31) **0.010**	1.22 (0.78-1.92) 0.384	1.32 (1.03-1.68) **0.026**	1.76 (1.01-3.09) **0.047**	1.89 (1.26-2.84) **0.001**	1.17 (0.72-1.89) 0.536	1.39 (1.07-1.81) **0.012**

OR, odds ratio; 95% CI, 95% confidence interval.

ORs and 95% CI in the multivariate analysis were adjusted for age, gender, *H. pylori* infection, smoking habit, and family history of GC.

P values < 0.05 are highlighted in bold.

Supplementary Table 7: Association of DNA repair gene polymorphisms with GC risk. Stratified analysis by age.

		Age < 50 years					Age > 50 years				
		Log-additive genetic model					Log-additive genetic model				
			95% CI					95% CI			
db SNP ID	Gen	OR[a]	Lower	Upper	*P*-value	FDR[b]	OR[a]	Lower	Upper	*P*-value	FDR[b]
rs10079641	*MSH3*	1.06	0.43	2.65	0.900	0.989	0.97	0.74	1.29	0.845	0.983
rs1042522	*TP53*	0.91	0.45	1.84	0.797	0.942	0.77	0.63	0.93	**0.006**	0.334
rs1047768	*ERCC5*	0.76	0.44	1.33	0.334	0.796	0.95	0.80	1.12	0.531	0.828
rs1047840	*EXO1*	1.10	0.87	1.39	0.431	0.975	0.85	0.72	1.01	0.066	0.509
rs1048771	*RAD54L*	1.04	0.71	1.52	0.839	0.796	1.09	0.83	1.44	0.524	0.828
rs1051677	*XRCC5*	0.75	0.33	1.71	0.317	0.796	1.18	0.87	1.60	0.276	0.766
rs1051685	*XRCC5*	0.61	0.27	1.42	0.230	0.796	1.09	0.83	1.44	0.533	0.828
rs1052133	*OGG1*	0.98	0.53	1.82	0.951	0.989	0.93	0.76	1.15	0.507	0.828
rs1059262	*ALKBH2*	1.08	0.51	2.27	0.849	0.975	0.90	0.73	1.11	0.319	0.771
rs1060915	*BRCA1*	1.24	0.67	2.29	0.497	0.839	1.09	0.91	1.30	0.374	0.776
rs11226	*RAD52*	1.29	0.67	2.50	0.448	0.839	1.21	1.01	1.43	**0.033**	0.477
rs1130409	*APEX1*	1.04	0.57	1.74	0.998	1	0.90	0.76	1.06	0.193	0.631
rs1136410	*PARP1*	1.55	0.66	3.63	0.394	0.805	1.18	0.92	1.52	0.181	0.616
rs13180316	*XRCC4*	1.51	0.81	2.82	0.186	0.796	0.96	0.8	1.16	0.687	0.916
rs13181	*ERCC2*	0.66	0.38	1.14	0.132	0.796	1.15	0.97	1.37	0.110	0.595
rs1346044	*WRN*	0.92	0.46	1.82	0.862	0.975	0.87	0.71	1.06	0.174	0.616
rs144848	*BRCA2*	1.02	0.56	1.85	0.944	0.989	1.10	0.91	1.33	0.310	0.771
rs1478485	*XRCC4*	0.68	0.38	1.21	0.187	0.796	1.14	0.96	1.35	0.144	0.616
rs1540354	*MLH1*	1.40	0.55	3.57	0.654	0.855	0.88	0.68	1.13	0.320	0.771
rs1614984	*TP53*	0.65	0.36	1.19	0.159	0.796	1.19	0.99	1.42	0.057	0.477
rs1618536	*ERCC2*	0.79	0.44	1.42	0.423	0.839	0.93	0.78	1.09	0.367	0.776
rs1650697	*MSH3*	0.96	0.51	1.80	0.904	0.989	0.91	0.74	1.10	0.321	0.771
rs174538	*FEN1*	0.99	0.51	1.92	0.977	0.996	0.99	0.83	1.20	0.953	0.983
rs175080	*MLH3*	0.86	0.49	1.50	0.585	0.845	1.04	0.88	1.23	0.628	0.871
rs1760944	*APEX1*	1.02	0.57	1.85	0.944	0.989	1.01	0.84	1.22	0.901	0.983
rs17655	*ERCC5*	1.16	0.65	2.05	0.617	0.855	0.79	0.65	0.96	**0.017**	0.477
rs176641	*POLG*	1.10	0.62	1.95	0.751	0.942	1.19	0.99	1.41	0.057	0.477
rs1776148	*EXO1*	1.28	0.73	2.26	0.388	0.805	0.96	0.81	1.14	0.626	0.871
rs1799793	*ERCC2*	0.76	0.45	1.28	0.300	0.796	1.15	0.96	1.37	0.131	0.616
rs1799794	*XRCC3*	0.79	0.41	1.50	0.465	0.839	0.94	0.78	1.14	0.556	0.828
rs1799796	*XRCC3*	0.72	0.36	1.43	0.345	0.796	0.91	0.75	1.12	0.373	0.776
rs1799801	*ERCC4*	0.75	0.42	1.34	0.325	0.796	0.92	0.77	1.10	0.343	0.776
rs1799955	*BRCA2*	0.92	0.47	1.80	0.799	0.942	0.98	0.79	1.20	0.827	0.983
rs1799966	*BRCA1*	1.24	0.67	2.29	0.497	0.839	1.05	0.88	1.26	0.609	0.871
rs1799977	*MLH1*	0.69	0.38	1.24	0.206	0.796	1.01	0.85	1.21	0.903	0.983
rs1800067	*ERCC4*	0.62	0.24	1.61	0.522	0.845	0.97	0.75	1.27	0.840	0.983
rs1800389	*WRN*	0.87	0.45	1.67	0.740	0.942	0.88	0.73	1.05	0.161	0.616
rs1800734	*MLH1*	1.39	0.74	2.62	0.301	0.796	0.99	0.81	1.19	0.881	0.983
rs1800935	*MSH6*	0.97	0.53	1.78	0.921	0.989	1.15	0.95	1.39	0.159	0.616
rs1800975	*XPA*	0.76	0.44	1.29	0.299	0.796	0.95	0.79	1.14	0.570	0.832
rs1801406	*BRCA2*	0.86	0.44	1.68	0.659	0.889	0.90	0.75	1.09	0.287	0.771
rs1801516	*ATM*	1.95	0.74	5.15	0.372	0.796	1.09	0.86	1.38	0.491	0.828
rs1802904	*ATR*	1.41	0.60	3.27	0.602	0.845	1.11	0.87	1.43	0.398	0.776
rs1805386	*LIG4*	0.98	0.47	2.01	0.949	0.989	0.97	0.77	1.22	0.785	0.983
rs1805388	*LIG4*	1.45	0.63	3.35	0.402	0.839	1.09	0.85	1.4	0.512	0.828
rs1805794	*NBS1*	1.29	0.74	2.25	0.368	0.796	1.02	0.86	1.22	0.798	0.983
rs1981928	*MSH2*	0.71	0.37	1.34	0.288	0.796	1.01	0.84	1.23	0.898	0.983
rs2020911	*MSH6*	0.93	0.51	1.68	0.802	0.942	0.98	0.82	1.16	0.801	0.983
rs2040639	*XRCC2*	1.46	0.85	2.51	0.172	0.796	0.85	0.72	1	0.053	0.477
rs2048718	*BRIP1*	1.10	0.62	1.98	0.737	0.942	0.93	0.78	1.1	0.402	0.776
rs20580	*LIG1*	1.22	0.74	2.04	0.435	0.839	1.06	0.9	1.25	0.473	0.828
rs2074522	*LIG3*	0.98	0.34	2.72	1	1	1.32	0.99	1.76	0.054	0.477
rs2075685	*XRCC4*	0.72	0.41	1.27	0.254	0.796	1.09	0.92	1.3	0.314	0.771
rs207906	*XRCC5*	0.65	0.29	1.45	0.288	0.796	1	0.77	1.28	0.974	0.983
rs2228000	*XPC*	0.70	0.38	1.29	0.251	0.796	0.83	0.69	0.99	**0.040**	0.477
rs2228001	*XPC*	0.91	0.51	1.63	0.757	0.942	0.99	0.84	1.18	0.953	0.983
rs2228006	*PMS2*	0.85	0.37	1.96	0.553	0.845	1.11	0.88	1.4	0.396	0.776

rs2238463	*ERCC4*	0.66	0.36	1.22	0.180	0.796	0.84	0.71	1	**0.049**	0.477
rs2252775	*RAD50*	1.20	0.58	2.46	0.262	0.796	1.01	0.82	1.26	0.895	0.983
rs2272615	*POLB*	0.62	0.27	1.38	0.348	0.796	1.01	0.78	1.30	0.948	0.983
rs2286940	*MLH1*	0.81	0.46	1.44	0.478	0.839	1.04	0.88	1.23	0.642	0.878
rs2303428	*MSH2*	1.76	0.81	3.81	0.178	0.796	1.09	0.82	1.44	0.560	0.828
rs2308321	*MGMT*	0.98	0.36	2.65	0.775	0.942	0.91	0.68	1.21	0.510	0.828
rs2345060	*PMS2*	0.65	0.34	1.23	0.177	0.796	0.86	0.71	1.05	0.146	0.616
rs2348244	*MSH6*	0.87	0.33	2.26	0.821	0.975	0.78	0.60	1.01	0.056	0.477
rs238406	*ERCC2*	1.28	0.76	2.15	0.349	0.796	1	0.85	1.18	0.968	0.983
rs2434470	*ALKBH3*	0.94	0.46	1.89	0.858	0.975	0.86	0.70	1.04	0.126	0.616
rs2440	*XRCC5*	1.73	0.95	3.18	0.070	0.796	0.99	0.83	1.17	0.890	0.983
rs25487	*XRCC1*	1.12	0.66	1.89	0.677	0.903	0.86	0.73	1.02	0.085	0.572
rs26279	*MSH3*	1.34	0.70	2.56	0.368	0.796	1	0.84	1.19	0.989	0.989
rs26779	*MSH3*	0.87	0.50	1.49	0.603	0.845	0.86	0.72	1.02	0.081	0.572
rs293794	*OGG1*	0.46	0.21	1.02	0.119	0.796	1.09	0.87	1.36	0.469	0.828
rs3136038	*ERCC4*	0.66	0.35	1.22	0.176	0.796	0.84	0.71	1.01	0.057	0.477
rs3136228	*MSH6*	1.17	0.68	1.99	0.574	0.845	1.08	0.91	1.29	0.387	0.776
rs3212948	*ERCC1*	0.86	0.50	1.48	0.579	0.845	1.02	0.86	1.21	0.807	0.983
rs3212961	*ERCC1*	0.98	0.43	2.23	0.821	0.954	1.08	0.84	1.40	0.556	0.828
rs3212986	*ERCC1*	0.81	0.43	1.52	0.505	0.839	1.01	0.83	1.23	0.906	0.983
rs3213245	*XRCC1*	0.70	0.37	1.34	0.280	0.796	1.11	0.94	1.31	0.206	0.637
rs3218536	*XRCC2*	1.50	0.66	3.39	0.571	0.845	1.01	0.76	1.35	0.942	0.983
rs3219489	*MUTYH*	0.69	0.36	1.35	0.277	0.796	0.92	0.76	1.12	0.398	0.776
rs3626	*PCNA*	1.55	0.66	3.64	0.570	0.845	0.89	0.69	1.15	0.372	0.776
rs3730668	*POLI*	1.22	0.70	2.13	0.476	0.839	0.96	0.81	1.14	0.665	0.898
rs3793784	*ERCC6*	0.72	0.42	1.24	0.233	0.796	0.94	0.79	1.11	0.440	0.805
rs4150416	*ERCC3*	1.12	0.61	2.06	0.715	0.930	0.82	0.68	0.98	**0.032**	0.477
rs4150441	*ERCC3*	0.73	0.41	1.28	0.270	0.796	1.12	0.94	1.33	0.207	0.637
rs4150474	*ERCC3*	0.92	0.48	1.75	0.797	0.942	0.87	0.71	1.06	0.156	0.616
rs4234259	*MLH1*	0.77	0.43	1.38	0.376	0.796	1.03	0.87	1.21	0.735	0.968
rs4253160	*ERCC6*	0.74	0.43	1.28	0.275	0.796	0.93	0.79	1.10	0.385	0.776
rs4968451	*BRIP1*	0.70	0.31	1.56	0.589	0.845	0.91	0.73	1.14	0.421	0.785
rs4986764	*BRIP1*	0.64	0.35	1.19	0.156	0.796	0.87	0.73	1.03	0.102	0.577
rs4987876	*ATM*	0.26	0.07	0.93	**0.049**	0.796	0.97	0.73	1.28	0.822	0.983
rs569143	*MRE11A*	0.72	0.43	1.20	0.204	0.796	0.90	0.76	1.07	0.224	0.655
rs5744934	*POLE*	0.98	0.48	1.98	0.953	0.989	1.06	0.85	1.31	0.629	0.871
rs601341	*MRE11A*	0.70	0.41	1.19	0.187	0.796	0.89	0.75	1.06	0.183	0.616
rs6413436	*RAD52*	1.18	0.64	2.19	0.601	0.845	1.14	0.96	1.36	0.135	0.616
rs664143	*ATM*	0.96	0.55	1.69	0.892	0.989	0.86	0.72	1.02	0.091	0.577
rs7182283	*NEIL1*	0.82	0.47	1.43	0.484	0.839	0.93	0.79	1.10	0.416	0.785
rs735943	*EXO1*	1.10	0.67	1.81	0.704	0.928	0.91	0.77	1.07	0.248	0.704
rs7797466	*PMS2*	2.02	0.93	4.38	0.136	0.796	1.03	0.82	1.29	0.816	0.983
rs799917	*BRCA1*	1.16	0.62	2.17	0.633	0.866	1.06	0.88	1.26	0.554	0.828
rs8305	*POLI*	1.57	0.79	3.13	0.197	0.796	1.12	0.93	1.35	0.224	0.655
rs861528	*XRCC3*	1.86	0.97	3.54	0.055	0.796	1.15	0.94	1.42	0.172	0.616
rs861531	*XRCC3*	1.37	0.76	2.48	0.289	0.796	1.06	0.89	1.26	0.530	0.828
rs861539	*XRCC3*	1.20	0.67	2.14	0.542	0.845	1.01	0.85	1.20	0.939	0.983
rs9350	*EXO1*	2.19	1.03	4.68	**0.035**	0.796	0.82	0.65	1.04	0.099	0.577
rs963248	*XRCC4*	1.22	0.57	2.57	0.242	0.796	1.01	0.81	1.27	0.908	0.983
rs9876116	*MLH1*	0.81	0.46	1.43	0.467	0.839	1	0.84	1.18	0.965	0.983
rs9894946	*TP53*	1.62	0.72	3.65	0.310	0.796	0.65	0.51	0.83	**0.001**	0.057

GC, gastric cancer; OR, odds ratio; CI, confidence interval.

[a]ORs adjusted by gender, *Helicobacter pylori* infection, smoking, and family history of gastric cancer.

[b]QFDR-values obtained after applying the False Discovery Rate (FDR) test.

P-values <0.05 are highlighted in bold.

Supplementary Table 8: Association of DNA repair polymorphisms with gastric cancer risk. Stratified analysis by gender.

		Female Gender					Male Gender				
		Log-additive genetic model					Log-additive genetic model				
			95% CI					95% CI			
db SNP ID	Gen	OR[a]	Lower	Upper	*P*-value	FDR[b]	OR[a]	Lower	Upper	*P*-value	FDR[b]
rs10079641	*MSH3*	0.86	0.53	1.39	0.538	0.966	1.04	0.75	1.43	0.816	0.997
rs1042522	*TP53*	0.79	0.55	1.13	0.190	0.875	0.72	0.49	1.05	0.092	0.588
rs1047768	*ERCC5*	0.89	0.67	1.20	0.449	0.966	0.95	0.78	1.15	0.579	0.914
rs1047840	*EXO1*	1.06	0.79	1.42	0.695	0.983	0.84	0.69	1.03	0.093	0.588
rs1048771	*RAD54L*	1.16	0.79	1.71	0.447	0.966	0.79	0.57	1.10	0.155	0.685
rs1051677	*XRCC5*	0.83	0.48	1.43	0.599	0.966	1.25	0.9	1.75	0.183	0.710
rs1051685	*XRCC5*	1.03	0.63	1.69	0.900	0.983	0.98	0.72	1.35	0.910	0.997
rs1052133	*OGG1*	0.96	0.68	1.36	0.817	0.983	0.93	0.73	1.17	0.529	0.914
rs1059262	*ALKBH2*	1.06	0.74	1.52	0.757	0.983	0.85	0.66	1.09	0.189	0.710
rs1060915	*BRCA1*	0.89	0.66	1.21	0.453	0.966	1.21	0.98	1.50	0.072	0.556
rs11226	*RAD52*	1.29	0.95	1.76	0.107	0.875	1.18	0.97	1.44	0.099	0.588
rs1130409	*APEX1*	1	0.76	1.31	0.999	0.999	0.86	0.71	1.04	0.125	0.612
rs1136410	*PARP1*	1.33	1.02	1.77	**0.044**	0.642	1.05	0.79	1.40	0.730	0.950
rs13180316	*XRCC4*	1.12	0.82	1.53	0.476	0.966	0.95	0.76	1.18	0.615	0.914
rs13181	*ERCC2*	1.21	0.9	1.62	0.216	0.875	1.05	0.86	1.28	0.641	0.917
rs1346044	*WRN*	0.97	0.67	1.39	0.854	0.983	0.84	0.66	1.05	0.130	0.612
rs144848	*BRCA2*	1.08	0.8	1.47	0.608	0.966	1.10	0.88	1.38	0.395	0.832
rs1478485	*XRCC4*	1.03	0.77	1.37	0.850	0.983	1.12	0.92	1.37	0.267	0.774
rs1540354	*MLH1*	1.07	0.68	1.69	0.761	0.983	0.85	0.64	1.13	0.266	0.774
rs1614984	*TP53*	1.12	0.86	1.45	0.407	0.944	1.03	0.83	1.26	0.802	0.997
rs1618536	*ERCC2*	1.18	0.89	1.57	0.258	0.875	0.95	0.78	1.15	0.595	0.914
rs1650697	*MSH3*	1.28	0.91	1.81	0.159	0.875	0.79	0.63	0.99	**0.039**	0.503
rs174538	*FEN1*	0.91	0.66	1.26	0.575	0.966	1.04	0.84	1.28	0.744	0.957
rs175080	*MLH3*	1.18	0.88	1.57	0.279	0.875	0.97	0.80	1.17	0.729	0.950
rs1760944	*APEX1*	0.99	0.72	1.37	0.969	0.983	1.02	0.83	1.26	0.855	0.997
rs17655	*ERCC5*	0.81	0.57	1.14	0.222	0.875	0.83	0.67	1.03	0.085	0.576
rs176641	*POLG*	1.06	0.78	1.43	0.730	0.983	1.23	1.01	1.51	**0.040**	0.503
rs1776148	*EXO1*	1.03	0.76	1.40	0.831	0.983	0.96	0.79	1.17	0.694	0.925
rs1799793	*ERCC2*	1.35	1.01	1.82	**0.047**	0.642	0.98	0.81	1.22	0.973	0.997
rs1799794	*XRCC3*	0.98	0.70	1.37	0.896	0.983	0.91	0.73	1.13	0.397	0.832
rs1799796	*XRCC3*	0.92	0.66	1.29	0.639	0.983	0.88	0.70	1.12	0.298	0.785
rs1799801	*ERCC4*	0.87	0.64	1.19	0.385	0.944	0.91	0.74	1.12	0.392	0.832
rs1799955	*BRCA2*	0.91	0.64	1.29	0.591	0.966	1.01	0.79	1.28	0.972	0.997
rs1799966	*BRCA1*	0.88	0.65	1.19	0.403	0.944	1.16	0.94	1.44	0.159	0.685
rs1799977	*MLH1*	0.91	0.68	1.22	0.537	0.966	1.01	0.82	1.25	0.901	0.997
rs1800067	*ERCC4*	0.99	0.63	1.56	0.974	0.983	0.92	0.68	1.25	0.588	0.914
rs1800389	*WRN*	0.87	0.64	1.18	0.366	0.944	0.89	0.72	1.11	0.312	0.801
rs1800734	*MLH1*	1.01	0.73	1.41	0.972	0.983	1.02	0.82	1.27	0.863	0.997
rs1800935	*MSH6*	1.01	0.73	1.40	0.963	0.983	1.19	0.95	1.48	0.122	0.612
rs1800975	*XPA*	0.90	0.66	1.21	0.473	0.966	0.94	0.77	1.16	0.575	0.914
rs1801406	*BRCA2*	0.88	0.64	1.21	0.420	0.944	0.91	0.73	1.14	0.408	0.832
rs1801516	*ATM*	1.13	0.77	1.66	0.537	0.966	1.12	0.84	1.5	0.427	0.854
rs1802904	*ATR*	1.20	0.78	1.85	0.399	0.944	1.1	0.83	1.47	0.497	0.886
rs1805386	*LIG4*	1.03	0.69	1.53	0.893	0.983	0.95	0.73	1.23	0.673	0.925
rs1805388	*LIG4*	1.06	0.68	1.64	0.800	0.983	1.14	0.86	1.53	0.365	0.832
rs1805794	*NBS1*	1.18	0.87	1.61	0.285	0.875	0.99	0.81	1.22	0.934	0.997
rs1981928	*MSH2*	0.93	0.66	1.32	0.698	0.983	1	0.81	1.25	0.980	0.997
rs2020911	*MSH6*	0.78	0.58	1.06	0.108	0.875	1.08	0.88	1.31	0.478	0.886
rs2040639	*XRCC2*	0.91	0.68	1.22	0.539	0.966	0.88	0.73	1.07	0.191	0.710
rs2048718	*BRIP1*	0.84	0.64	1.12	0.234	0.875	1.01	0.81	1.23	0.991	0.997
rs20580	*LIG1*	0.82	0.62	1.09	0.168	0.875	1.22	1.01	1.47	**0.042**	0.503
rs2074522	*LIG3*	1.27	0.88	1.84	0.197	0.875	1.13	0.8	1.59	0.500	0.886
rs2075685	*XRCC4*	1.14	0.85	1.53	0.381	0.944	1.02	0.83	1.24	0.870	0.997
rs207906	*XRCC5*	0.89	0.57	1.39	0.608	0.966	0.99	0.74	1.31	0.927	0.997
rs2228000	*XPC*	0.78	0.57	1.08	0.133	0.875	0.83	0.68	1.02	0.077	0.556
rs2228001	*XPC*	0.84	0.62	1.13	0.252	0.875	1.06	0.87	1.3	0.559	0.914
rs2228006	*PMS2*	1.32	0.87	2.01	0.184	0.875	0.99	0.77	1.31	0.997	0.997

rs2238463	*ERCC4*	0.85	0.63	1.15	0.301	0.878	0.81	0.66	0.99	**0.042**	0.503
rs2252775	*RAD50*	0.85	0.58	1.23	0.384	0.944	1.12	0.87	1.43	0.378	0.832
rs2272615	*POLB*	1.13	0.72	1.77	0.592	0.966	0.9	0.67	1.2	0.475	0.886
rs2286940	*MLH1*	0.98	0.75	1.29	0.889	0.983	1.04	0.86	1.27	0.686	0.925
rs2303428	*MSH2*	1.01	0.63	1.63	0.960	0.983	1.22	0.89	1.66	0.216	0.728
rs2308321	*MGMT*	0.89	0.52	1.52	0.834	0.983	0.92	0.67	1.28	0.625	0.914
rs2345060	*PMS2*	0.91	0.64	1.28	0.571	0.966	0.82	0.65	1.02	0.077	0.556
rs2348244	*MSH6*	0.66	0.43	0.99	**0.048**	0.642	0.86	0.64	1.17	0.350	0.832
rs238406	*ERCC2*	1.06	0.81	1.39	0.681	0.983	1.06	0.88	1.27	0.569	0.914
rs2434470	*ALKBH3*	0.81	0.57	1.17	0.259	0.875	0.88	0.7	1.11	0.272	0.774
rs2440	*XRCC5*	1.10	0.82	1.46	0.525	0.966	10.1	0.82	1.22	0.996	0.997
rs25487	*XRCC1*	1.03	0.77	1.37	0.839	0.983	0.83	0.68	1.02	0.051	0.504
rs26279	*MSH3*	1.18	0.88	1.59	0.269	0.875	0.95	0.78	1.16	0.623	0.914
rs26779	*MSH3*	0.97	0.72	1.31	0.864	0.983	0.81	0.66	0.99	**0.038**	0.503
rs293794	*OGG1*	0.85	0.57	1.26	0.420	0.944	1.10	0.85	1.42	0.489	0.886
rs3136038	*ERCC4*	0.85	0.62	1.15	0.292	0.875	0.82	0.66	10.2	0.051	0.504
rs3136228	*MSH6*	0.99	0.73	1.33	0.939	0.983	1.14	0.93	1.40	0.204	0.712
rs3212948	*ERCC1*	1.15	0.86	1.55	0.343	0.944	0.95	0.78	1.15	0.583	0.914
rs3212961	*ERCC1*	1.27	0.81	1.99	0.152	0.875	0.99	0.74	1.33	0.971	0.997
rs3212986	*ERCC1*	1.22	0.87	1.73	0.248	0.875	0.91	0.73	1.14	0.401	0.832
rs3213245	*XRCC1*	1.01	0.75	1.36	0.954	0.983	1.11	0.92	1.34	0.280	0.774
rs3218536	*XRCC2*	1.01	0.61	1.65	0.847	0.983	1.08	0.78	1.49	0.645	0.917
rs3219489	*MUTYH*	0.83	0.59	1.15	0.262	0.875	0.93	0.75	1.17	0.552	0.914
rs3626	*PCNA*	0.94	0.62	1.42	0.773	0.983	0.93	0.69	1.25	0.627	0.914
rs3730668	*POLI*	0.99	0.73	1.35	0.967	0.983	0.98	0.80	1.19	0.835	0.997
rs3793784	*ERCC6*	0.95	0.72	1.25	0.719	0.983	0.9	0.73	1.09	0.274	0.774
rs4150416	*ERCC3*	1.23	0.98	1.56	0.075	0.833	0.97	0.79	1.20	0.796	0.997
rs4150441	*ERCC3*	1.23	0.91	1.67	0.177	0.875	1.02	0.84	1.24	0.865	0.997
rs4150474	*ERCC3*	1.21	0.95	1.55	0.119	0.875	1.02	0.81	1.28	0.880	0.997
rs4234259	*MLH1*	0.94	0.72	1.24	0.676	0.983	1.04	0.86	1.27	0.686	0.925
rs4253160	*ERCC6*	0.87	0.66	1.15	0.319	0.908	0.93	0.77	1.13	0.481	0.886
rs4968451	*BRIP1*	0.90	0.64	1.28	0.569	0.966	0.89	0.67	1.17	0.396	0.832
rs4986764	*BRIP1*	0.79	0.59	1.06	0.112	0.875	0.88	0.72	1.07	0.199	0.712
rs4987876	*ATM*	1.24	0.78	1.98	0.368	0.944	0.77	0.55	1.07	0.119	0.612
rs569143	*MRE11A*	1.04	0.78	1.38	0.781	0.983	1.23	1.01	1.50	**0.036**	0.503
rs5744934	*POLE*	1.14	0.79	1.63	0.485	0.966	1.01	0.78	1.30	0.965	0.997
rs601341	*MRE11A*	1.06	0.79	1.42	0.714	0.983	1.10	0.86	1.41	0.462	0.886
rs6413436	*RAD52*	1.19	0.87	1.62	0.272	0.875	1.13	0.92	1.37	0.240	0.773
rs664143	*ATM*	0.80	0.60	1.08	0.144	0.875	0.90	0.74	1.11	0.325	0.816
rs7182283	*NEIL1*	0.94	0.70	1.25	0.653	0.983	0.92	0.76	1.11	0.381	0.832
rs735943	*EXO1*	0.98	0.75	1.32	0.974	0.983	0.89	0.74	1.08	0.243	0.773
rs7797466	*PMS2*	1.25	0.84	1.85	0.272	0.875	1.02	0.79	1.33	0.858	0.997
rs799917	*BRCA1*	0.84	0.62	1.14	0.259	0.875	1.19	0.96	1.47	0.104	0.588
rs8305	*POLI*	0.98	0.71	1.36	0.907	0.983	1.23	0.99	1.53	0.057	0.517
rs861528	*XRCC3*	1.39	0.97	1.98	0.069	0.833	1.13	0.9	1.43	0.298	0.785
rs861531	*XRCC3*	1.08	0.81	1.46	0.596	0.966	1.08	0.88	1.32	0.461	0.886
rs861539	*XRCC3*	1.03	0.77	1.38	0.837	0.983	1.02	0.83	1.24	0.869	0.997
rs9350	*EXO1*	1.10	0.74	1.65	0.640	0.983	0.83	0.64	1.08	0.165	0.685
rs963248	*XRCC4*	0.97	0.65	1.43	0.866	0.983	1.06	0.82	1.37	0.675	0.925
rs9876116	*MLH1*	0.93	0.71	1.21	0.576	0.966	1.01	0.83	1.23	0.919	0.997
rs9894946	*TP53*	0.78	0.51	1.20	0.158	0.875	0.77	0.62	0.96	**0.017**	0.503

OR, odds ratio; CI, confidence interval.

[a]ORs adjusted by age, *Helicobacter pylori* infection, smoking status, and family history of gastric cancer.

[b]QFDR-values obtained after applying the False Discovery Rate (FDR) test.

P-values <0.05 are highlighted in bold.

Supplementary Table 9: Association of DNA repair gene polymorphisms with gastric cancer risk. Stratified analysis by smoking status (never smokers / current smokers).

		Never smokers					Current smokers				
		Log-additive genetic model					Log-additive genetic model				
			95% CI					95% CI			
db SNP ID	Gen	OR[a]	Lower	Upper	*P*-value	FDR[b]	OR[a]	Lower	Upper	*P*-value	FDR[b]
rs10079641	*MSH3*	0.90	0.62	1.33	0.611	0.957	1.50	0.80	2.83	0.195	0.994
rs1042522	*TP53*	0.81	0.62	1.06	0.124	0.810	0.60	0.38	0.96	**0.031**	0.943
rs1047768	*ERCC5*	0.88	0.71	1.10	0.276	0.927	1.02	0.71	1.48	0.900	0.994
rs1047840	*EXO1*	0.81	0.64	1.02	0.076	0.810	1.11	0.75	1.66	0.600	0.994
rs1048771	*RAD54L*	1.24	0.87	1.76	0.232	0.927	0.79	0.40	1.57	0.568	0.994
rs1051677	*XRCC5*	1.39	0.91	2.12	0.173	0.810	0.76	0.40	1.45	0.477	0.994
rs1051685	*XRCC5*	1.01	0.69	1.45	0.989	0.990	0.90	0.46	1.73	0.743	0.994
rs1052133	*OGG1*	0.86	0.65	1.13	0.274	0.927	1.09	0.67	1.78	0.720	0.994
rs1059262	*ALKBH2*	0.90	0.67	1.21	0.492	0.949	1.10	0.68	1.78	0.689	0.994
rs1060915	*BRCA1*	1.09	0.85	1.39	0.492	0.949	1.01	0.67	1.51	0.965	0.994
rs11226	*RAD52*	1.25	0.98	1.58	0.072	0.810	1.31	0.87	1.96	0.188	0.994
rs1130409	*APEX1*	0.93	0.75	1.16	0.518	0.949	0.80	0.54	1.19	0.267	0.994
rs1136410	*PARP1*	1.36	0.97	1.91	0.076	0.810	0.91	0.52	1.58	0.727	0.994
rs13180316	*XRCC4*	0.97	0.76	1.23	0.782	0.987	0.91	0.58	1.44	0.702	0.994
rs13181	*ERCC2*	1.15	0.91	1.46	0.234	0.927	1.03	0.69	1.55	0.884	0.994
rs1346044	*WRN*	0.96	0.72	1.27	0.765	0.987	1.03	0.65	1.61	0.907	0.994
rs144848	*BRCA2*	1.06	0.82	1.37	0.641	0.976	1.10	0.72	1.69	0.653	0.994
rs1478485	*XRCC4*	1.15	0.91	1.44	0.243	0.927	0.95	0.63	1.41	0.785	0.994
rs1540354	*MLH1*	0.85	0.60	1.21	0.362	0.949	1.15	0.65	2.04	0.631	0.994
rs1614984	*TP53*	1.20	0.94	1.53	0.148	0.810	0.79	0.52	1.21	0.283	0.994
rs1618536	*ERCC2*	1.13	0.90	1.42	0.280	0.927	0.83	0.55	1.24	0.358	0.994
rs1650697	*MSH3*	1	0.77	1.30	0.990	0.990	0.58	0.37	0.91	**0.016**	0.943
rs174538	*FEN1*	0.99	0.77	1.28	0.963	0.987	0.98	0.64	1.49	0.918	0.994
rs175080	*MLH3*	1.01	0.80	1.27	0.943	0.987	0.92	0.64	1.34	0.676	0.994
rs1760944	*APEX1*	0.95	0.75	1.22	0.707	0.979	1.11	0.71	1.74	0.651	0.994
rs17655	*ERCC5*	0.77	0.59	1.01	0.058	0.810	1.01	0.66	1.54	0.963	0.994
rs176641	*POLG*	1.08	0.85	1.37	0.554	0.949	1.58	1.04	2.42	0.031	0.943
rs1776148	*EXO1*	1.01	0.80	1.29	0.914	0.987	1.09	0.74	1.62	0.662	0.994
rs1799793	*ERCC2*	1.14	0.90	1.46	0.270	0.927	1.16	0.77	1.77	0.476	0.994
rs1799794	*XRCC3*	0.95	0.73	1.23	0.679	0.979	0.87	0.57	1.33	0.517	0.994
rs1799796	*XRCC3*	1.01	0.78	1.32	0.926	0.987	0.89	0.55	1.44	0.629	0.994
rs1799801	*ERCC4*	0.93	0.73	1.18	0.536	0.949	0.82	0.55	1.25	0.360	0.994
rs1799955	*BRCA2*	0.99	0.75	1.30	0.918	0.987	1.05	0.64	1.72	0.839	0.994
rs1799966	*BRCA1*	1.05	0.82	1.34	0.701	0.979	1.01	0.67	1.51	0.965	0.994
rs1799977	*MLH1*	0.99	0.78	1.25	0.915	0.987	0.9	0.61	1.34	0.608	0.994
rs1800067	*ERCC4*	0.95	0.67	1.33	0.756	0.987	1.02	0.54	1.92	0.957	0.994
rs1800389	*WRN*	0.98	0.76	1.25	0.861	0.987	0.94	0.57	1.54	0.799	0.994
rs1800734	*MLH1*	0.95	0.73	1.23	0.673	0.979	1.07	0.69	1.65	0.769	0.994
rs1800935	*MSH6*	1.09	0.83	1.42	0.541	0.949	1.06	0.70	1.62	0.769	0.994
rs1800975	*XPA*	0.91	0.71	1.15	0.425	0.949	0.82	0.54	1.24	0.338	0.994
rs1801406	*BRCA2*	0.99	0.77	1.29	0.969	0.987	1.02	0.65	1.59	0.943	0.994
rs1801516	*ATM*	0.90	0.65	1.25	0.536	0.949	1.47	0.83	2.62	0.293	0.994
rs1802904	*ATR*	1.18	0.85	1.65	0.318	0.949	1.35	0.72	2.52	0.536	0.994
rs1805386	*LIG4*	0.98	0.72	1.34	0.895	0.987	0.81	0.48	1.36	0.424	0.994
rs1805388	*LIG4*	1.36	0.96	1.91	0.079	0.810	0.91	0.50	1.65	0.133	0.994
rs1805794	*NBS1*	1.07	0.84	1.35	0.603	0.957	1.03	0.69	1.55	0.872	0.994
rs1981928	*MSH2*	0.98	0.75	1.28	0.884	0.987	0.76	0.50	1.14	0.176	0.994
rs2020911	*MSH6*	0.92	0.73	1.17	0.501	0.949	0.99	0.66	1.47	0.950	0.994
rs2040639	*XRCC2*	0.92	0.74	1.16	0.491	0.949	1.01	0.67	1.49	0.995	0.995
rs2048718	*BRIP1*	1.11	0.89	1.39	0.362	0.949	1.01	0.67	1.52	0.972	0.994
rs20580	*LIG1*	1.08	0.87	1.35	0.493	0.949	1.28	0.88	1.87	0.194	0.994
rs2074522	*LIG3*	1.34	0.91	1.97	0.136	0.810	1.59	0.81	3.12	0.325	0.994
rs2075685	*XRCC4*	1.11	0.88	1.39	0.397	0.949	0.96	0.65	1.43	0.848	0.994
rs207906	*XRCC5*	0.79	0.56	1.10	0.156	0.810	1.08	0.58	2.01	0.408	0.994
rs2228000	*XPC*	0.81	0.63	1.05	0.105	0.810	0.83	0.56	1.21	0.324	0.994
rs2228001	*XPC*	0.88	0.69	1.11	0.280	0.927	1.09	0.74	1.62	0.667	0.994
rs2228006	*PMS2*	1.26	0.92	1.73	0.150	0.810	0.85	0.51	1.40	0.517	0.994

rs2238463	*ERCC4*	0.91	0.72	1.15	0.412	0.949	0.67	0.45	1	**0.048**	0.943
rs2252775	*RAD50*	0.92	0.69	1.24	0.595	0.957	1.16	0.7	1.93	0.557	0.994
rs2272615	*POLB*	1.08	0.76	1.53	0.675	0.979	0.84	0.48	1.50	0.566	0.994
rs2286940	*MLH1*	1.10	0.89	1.37	0.377	0.949	0.92	0.63	1.36	0.689	0.994
rs2303428	*MSH2*	0.89	0.60	1.31	0.552	0.949	0.98	0.59	1.63	0.941	0.994
rs2308321	*MGMT*	1.02	0.69	1.52	0.908	0.987	1.03	0.52	2.03	0.159	0.994
rs2345060	*PMS2*	0.92	0.70	1.19	0.517	0.949	0.75	0.47	1.19	0.219	0.994
rs2348244	*MSH6*	0.71	0.50	1.01	0.054	0.810	1.19	0.64	2.23	0.584	0.994
rs238406	*ERCC2*	1.01	0.81	1.25	0.945	0.987	1.03	0.69	1.52	0.896	0.994
rs2434470	*ALKBH3*	0.78	0.59	1.04	0.089	0.810	0.74	0.49	1.13	0.162	0.994
rs2440	*XRCC5*	1.02	0.81	1.27	0.887	0.987	1.34	0.90	2	0.142	0.994
rs25487	*XRCC1*	0.92	0.74	1.15	0.460	0.949	0.77	0.53	1.11	0.160	0.994
rs26279	*MSH3*	1.09	0.86	1.37	0.486	0.949	0.95	0.64	1.43	0.820	0.994
rs26779	*MSH3*	0.92	0.73	1.17	0.505	0.949	0.67	0.45	1.01	0.052	0.943
rs293794	*OGG1*	1.03	0.75	1.40	0.873	0.987	0.80	0.47	1.36	0.411	0.994
rs3136038	*ERCC4*	0.91	0.71	1.15	0.414	0.949	0.66	0.44	0.99	**0.043**	0.943
rs3136228	*MSH6*	1.04	0.82	1.32	0.757	0.987	0.98	0.66	1.44	0.906	0.994
rs3212948	*ERCC1*	1.05	0.83	1.31	0.703	0.979	1.10	0.73	1.65	0.665	0.994
rs3212961	*ERCC1*	1.10	0.77	1.58	0.595	0.957	1.30	0.74	2.27	0.362	0.994
rs3212986	*ERCC1*	1.09	0.83	1.44	0.517	0.949	0.93	0.58	1.50	0.777	0.994
rs3213245	*XRCC1*	1.01	0.81	1.27	0.929	0.987	1.27	0.86	1.88	0.228	0.994
rs3218536	*XRCC2*	1.06	0.71	1.57	0.407	0.949	0.81	0.44	1.47	0.097	0.994
rs3219489	*MUTYH*	0.80	0.62	1.05	0.108	0.810	1.12	0.71	1.75	0.631	0.994
rs3626	*PCNA*	0.98	0.69	1.39	0.909	0.987	0.8	0.43	1.49	0.697	0.994
rs3730668	*POLI*	0.91	0.72	1.15	0.423	0.949	0.99	0.66	1.48	0.955	0.994
rs3793784	*ERCC6*	0.93	0.75	1.16	0.538	0.949	0.71	0.48	1.06	0.096	0.994
rs4150416	*ERCC3*	0.74	0.57	0.94	**0.015**	0.796	0.91	0.60	1.36	0.637	0.994
rs4150441	*ERCC3*	1.14	0.90	1.44	0.283	0.927	1.02	0.69	1.52	0.906	0.994
rs4150474	*ERCC3*	0.86	0.70	1.12	0.215	0.927	0.92	0.60	1.41	0.696	0.994
rs4234259	*MLH1*	0.92	0.74	1.14	0.431	0.949	0.94	0.64	1.38	0.751	0.994
rs4253160	*ERCC6*	0.89	0.71	1.11	0.313	0.949	0.72	0.48	1.06	0.096	0.994
rs4968451	*BRIP1*	1.06	0.80	1.42	0.684	0.979	0.74	0.42	1.31	0.306	0.994
rs4986764	*BRIP1*	0.84	0.67	1.05	0.132	0.810	0.96	0.64	1.44	0.833	0.994
rs4987876	*ATM*	1.29	0.89	1.87	0.171	0.810	0.63	0.33	1.22	0.170	0.994
rs569143	*MRE11A*	0.93	0.74	1.17	0.532	0.949	0.78	0.53	1.15	0.210	0.994
rs5744934	*POLE*	1.04	0.77	1.40	0.798	0.987	1.18	0.70	2	0.093	0.994
rs601341	*MRE11A*	0.93	0.74	1.18	0.566	0.955	0.81	0.55	1.20	0.297	0.994
rs6413436	*RAD52*	1.19	0.94	1.50	0.160	0.810	1.05	0.69	1.59	0.813	0.994
rs664143	*ATM*	0.82	0.65	1.04	0.108	0.810	0.98	0.67	1.44	0.913	0.994
rs7182283	*NEIL1*	0.96	0.76	1.22	0.757	0.987	0.81	0.56	1.17	0.266	0.994
rs735943	*EXO1*	0.97	0.78	1.22	0.823	0.987	1	0.70	1.44	0.985	0.994
rs7797466	*PMS2*	0.93	0.68	1.27	0.629	0.970	0.99	0.63	1.57	0.977	0.994
rs799917	*BRCA1*	1.04	0.82	1.33	0.724	0.987	1.10	0.73	1.64	0.650	0.994
rs8305	*POLI*	1.17	0.90	1.51	0.234	0.927	0.98	0.65	1.48	0.924	0.994
rs861528	*XRCC3*	1.24	0.94	1.63	0.131	0.810	1.14	0.72	1.81	0.564	0.994
rs861531	*XRCC3*	1.01	0.79	1.28	0.965	0.987	1.24	0.84	1.84	0.275	0.994
rs861539	*XRCC3*	0.97	0.77	1.23	0.797	0.987	1.17	0.79	1.73	0.437	0.994
rs9350	*EXO1*	0.98	0.71	1.34	0.883	0.987	0.81	0.49	1.32	0.399	0.994
rs963248	*XRCC4*	0.97	0.71	1.33	0.869	0.987	1.19	0.73	1.93	0.489	0.994
rs9876116	*MLH1*	1.06	0.85	1.31	0.597	0.957	0.87	0.59	1.28	0.467	0.994
rs9894946	*TP53*	0.69	0.49	0.97	**0.033**	0.810	0.88	0.53	1.47	0.636	0.994

OR, odds ratio; CI, confidence interval.

[a]ORs adjusted by gender, age, *Helicobacter pylori* infection, and family history of gastric cancer.

[b]QFDR-values obtained after applying the False Discovery Rate (FDR) test.

P-values <0.05 are highlighted in bold.

Supplementary Table 10: Association of DNA repair gene polymorphisms with gastric cancer risk. Stratified analysis by family history of gastric cancer.

		Family history of GC (negative)					Family history of GC (positive)				
		Log-additive genetic model					Log-additive genetic model				
			95% CI					95% CI			
db SNP ID	Gen	OR[a]	Lower	Upper	*P*-value	FDR[b]	OR[a]	Lower	Upper	*P*-value	FDR[b]
rs10079641	*MSH3*	1.08	0.80	1.46	0.609	0.936	0.70	0.29	1.70	0.501	0.840
rs1042522	*TP53*	0.82	0.66	1.01	0.056	0.473	0.58	0.31	1.07	0.083	0.709
rs1047768	*ERCC5*	0.96	0.81	1.15	0.677	0.936	1.03	0.58	1.83	0.916	1
rs1047840	*EXO1*	0.88	0.73	1.07	0.194	0.626	1.03	0.57	1.87	0.926	1
rs1048771	*RAD54L*	1.06	0.79	1.41	0.714	0.952	1.19	0.41	3.46	1	1
rs1051677	*XRCC5*	1.23	0.90	1.69	0.195	0.626	0.73	0.26	2.04	0.585	0.867
rs1051685	*XRCC5*	0.97	0.72	1.31	0.832	0.992	1.54	0.50	4.76	0.071	0.709
rs1052133	*OGG1*	1.06	0.85	1.32	0.617	0.936	1.08	0.82	1.41	0.592	0.867
rs1059262	*ALKBH2*	0.92	0.73	1.16	0.494	0.889	0.81	0.39	1.66	0.564	0.867
rs1060915	*BRCA1*	1.05	0.86	1.28	0.616	0.936	1.23	0.66	2.28	0.514	0.840
rs11226	*RAD52*	1.13	0.87	1.46	0.360	0.806	0.79	0.45	1.39	0.408	0.819
rs1130409	*APEX1*	0.85	0.71	1.01	0.070	0.473	1.41	0.81	2.45	0.217	0.757
rs1136410	*PARP1*	1.19	0.90	1.57	0.220	0.626	1.52	0.67	3.46	0.672	0.931
rs13180316	*XRCC4*	1.01	0.82	1.23	0.987	0.992	1.21	0.62	2.37	0.570	0.867
rs13181	*ERCC2*	1.07	0.89	1.28	0.483	0.888	1.24	0.66	2.32	0.508	0.840
rs1346044	*WRN*	0.91	0.73	1.13	0.395	0.806	1.06	0.49	2.28	0.885	1
rs144848	*BRCA2*	1.15	0.94	1.41	0.167	0.626	1.18	0.56	2.47	0.859	1
rs1478485	*XRCC4*	1.01	0.84	1.21	0.931	0.992	1.10	0.61	1.97	0.746	0.956
rs1540354	*MLH1*	0.96	0.73	1.26	0.746	0.971	0.59	0.24	1.45	0.252	0.757
rs1614984	*TP53*	1.11	0.92	1.35	0.267	0.642	1.47	0.81	2.67	0.194	0.757
rs1618536	*ERCC2*	0.91	0.76	1.09	0.287	0.659	1.34	0.75	2.39	0.326	0.783
rs1650697	*MSH3*	0.87	0.71	1.08	0.203	0.626	1.18	0.60	2.35	0.625	0.913
rs174538	*FEN1*	1.01	0.83	1.23	0.924	0.992	0.89	0.47	1.71	0.731	0.956
rs175080	*MLH3*	0.99	0.83	1.18	0.907	0.992	1.59	0.88	2.87	0.114	0.709
rs1760944	*APEX1*	0.97	0.79	1.19	0.769	0.980	1.53	0.81	2.92	0.183	0.757
rs17655	*ERCC5*	0.89	0.73	1.09	0.273	0.642	0.53	0.25	1.08	0.081	0.709
rs176641	*POLG*	1.06	0.83	1.35	0.634	0.936	0.97	0.53	1.79	0.933	1
rs1776148	*EXO1*	1.06	0.87	1.28	0.568	0.936	1.50	0.82	2.72	0.177	0.757
rs1799793	*ERCC2*	1.09	0.90	1.32	0.386	0.806	0.74	0.42	1.32	0.309	0.783
rs1799794	*XRCC3*	0.88	0.71	1.08	0.219	0.626	2.07	0.90	4.74	0.265	0.757
rs1799796	*XRCC3*	0.96	0.77	1.20	0.737	0.971	0.53	0.26	1.06	0.072	0.709
rs1799801	*ERCC4*	0.89	0.74	1.08	0.255	0.642	0.79	0.42	1.48	0.465	0.840
rs1799955	*BRCA2*	1.05	0.84	1.31	0.693	0.936	0.47	0.21	1.02	0.062	0.709
rs1799966	*BRCA1*	1.02	0.84	1.24	0.860	0.992	1.22	0.66	2.26	0.528	0.851
rs1799977	*MLH1*	0.96	0.79	1.16	0.661	0.936	1.34	0.66	2.72	0.427	0.824
rs1800067	*ERCC4*	0.81	0.61	1.08	0.150	0.624	1.46	0.58	3.68	0.736	0.956
rs1800389	*WRN*	0.89	0.73	1.09	0.257	0.642	0.66	0.35	1.24	0.197	0.757
rs1800734	*MLH1*	1.01	0.82	1.24	0.933	0.992	0.92	0.47	1.81	0.816	1
rs1800935	*MSH6*	1.14	0.93	1.41	0.212	0.626	0.66	0.36	1.20	0.175	0.757
rs1800975	*XPA*	0.89	0.74	1.08	0.244	0.642	0.73	0.39	1.37	0.333	0.783
rs1801406	*BRCA2*	0.87	0.70	1.06	0.169	0.626	0.92	0.44	1.96	0.834	1
rs1801516	*ATM*	1.21	0.94	1.57	0.144	0.624	0.84	0.37	1.88	0.677	0.931
rs1802904	*ATR*	1.26	0.96	1.64	0.096	0.546	0.95	0.44	2.03	0.478	0.840
rs1805386	*LIG4*	1.03	0.81	1.32	0.804	0.992	0.97	0.43	2.17	0.326	0.783
rs1805388	*LIG4*	1.06	0.81	1.39	0.693	0.936	3.24	1.06	9.87	0.100	0.709
rs1805794	*NBS1*	1.05	0.87	1.27	0.633	0.936	1.25	0.66	2.37	0.491	0.840
rs1981928	*MSH2*	1.02	0.81	1.22	0.967	0.992	0.99	0.51	1.96	0.986	1
rs2020911	*MSH6*	0.99	0.82	1.20	0.958	0.992	0.98	0.55	1.76	0.957	1
rs2040639	*XRCC2*	0.93	0.77	1.11	0.395	0.806	0.97	0.55	1.71	0.918	1
rs2048718	*BRIP1*	0.98	0.82	1.18	0.850	0.992	1.38	0.70	2.72	0.344	0.791
rs20580	*LIG1*	1.18	0.99	1.41	0.067	0.473	0.76	0.44	1.31	0.326	0.783
rs2074522	*LIG3*	1.19	0.87	1.62	0.270	0.642	1.34	0.52	3.43	1	1
rs2075685	*XRCC4*	0.94	0.78	1.13	0.517	0.916	1.33	0.72	2.44	0.358	0.805
rs207906	*XRCC5*	0.84	0.64	1.10	0.209	0.626	1.20	0.49	2.93	0.686	0.938
rs2228000	*XPC*	0.82	0.68	0.99	**0.048**	0.473	1.08	0.54	2.18	0.821	1
rs2228001	*XPC*	1.05	0.87	1.26	0.620	0.936	0.74	0.42	1.32	0.307	0.783
rs2228006	*PMS2*	1.02	0.79	1.32	0.875	0.992	0.93	0.45	1.94	0.244	0.757

rs2238463	*ERCC4*	0.84	0.69	1.01	0.061	0.473	0.62	0.34	1.14	0.123	0.709
rs2252775	*RAD50*	1.01	0.80	1.26	0.971	0.992	1.40	0.65	2.99	0.377	0.814
rs2272615	*POLB*	0.92	0.70	1.20	0.535	0.931	0.68	0.30	1.55	0.367	0.810
rs2286940	*MLH1*	1.07	0.89	1.27	0.485	0.888	1.21	0.64	2.29	0.548	0.858
rs2303428	*MSH2*	1.14	0.86	1.51	0.377	0.806	0.96	0.38	2.44	0.253	0.757
rs2308321	*MGMT*	0.89	0.65	1.22	0.482	0.888	1.22	0.42	3.47	0.800	0.939
rs2345060	*PMS2*	0.92	0.74	1.13	0.416	0.832	0.56	0.28	1.14	0.109	0.709
rs2348244	*MSH6*	0.81	0.61	1.07	0.145	0.624	1.47	0.53	4.13	0.629	0.913
rs238406	*ERCC2*	0.98	0.82	1.16	0.785	0.986	1.41	0.81	2.45	0.217	0.757
rs2434470	*ALKBH3*	0.88	0.71	1.09	0.251	0.642	0.60	0.31	1.15	0.162	0.709
rs2440	*XRCC5*	1.08	0.90	1.29	0.434	0.852	1.02	0.56	1.85	0.956	1
rs25487	*XRCC1*	0.88	0.73	1.05	0.144	0.624	0.89	0.50	1.60	0.704	0.939
rs26279	*MSH3*	0.99	0.83	1.21	0.989	0.992	1.04	0.58	1.85	0.894	1
rs26779	*MSH3*	0.85	0.70	1.02	0.077	0.490	0.94	0.52	1.72	0.845	1
rs293794	*OGG1*	1.01	0.80	1.28	0.925	0.992	0.83	0.37	1.86	0.648	0.922
rs3136038	*ERCC4*	0.81	0.67	0.98	**0.034**	0.473	0.72	0.40	1.32	0.289	0.779
rs3136228	*MSH6*	1.09	0.90	1.33	0.358	0.805	0.80	0.44	1.44	0.454	0.840
rs3212948	*ERCC1*	1.03	0.85	1.24	0.771	0.980	0.70	0.40	1.24	0.222	0.757
rs3212961	*ERCC1*	1.20	0.91	1.59	0.202	0.626	0.57	0.26	1.24	0.163	0.757
rs3212986	*ERCC1*	0.98	0.79	1.22	0.869	0.992	0.76	0.39	1.46	0.409	0.819
rs3213245	*XRCC1*	1.17	0.97	1.40	0.096	0.546	1.24	0.68	2.26	0.477	0.840
rs3218536	*XRCC2*	1.08	0.79	1.46	0.643	0.936	0.51	0.22	1.16	0.114	0.709
rs3219489	*MUTYH*	1.06	0.86	1.31	0.592	0.936	1.11	0.87	1.41	0.392	0.814
rs3626	*PCNA*	0.93	0.71	1.23	0.628	0.936	0.70	0.32	1.53	0.227	0.757
rs3730668	*POLI*	0.88	0.72	1.06	0.169	0.626	0.73	0.42	1.25	0.242	0.757
rs3793784	*ERCC6*	0.84	0.70	1.01	0.065	0.473	1.14	0.63	2.04	0.665	0.931
rs4150416	*ERCC3*	0.83	0.68	1.01	0.067	0.473	0.62	0.32	1.20	0.151	0.757
rs4150441	*ERCC3*	1.04	0.87	1.25	0.662	0.936	1.66	0.86	3.19	0.125	0.709
rs4150474	*ERCC3*	0.87	0.71	1.08	0.210	0.626	0.68	0.35	1.36	0.278	0.768
rs4234259	*MLH1*	1.05	0.88	1.25	0.618	0.936	1.30	0.70	2.43	0.405	0.819
rs4253160	*ERCC6*	0.83	0.69	0.99	**0.041**	0.473	0.98	0.57	1.69	0.951	1
rs4968451	*BRIP1*	0.90	0.70	1.15	0.389	0.806	0.97	0.43	2.18	0.814	1
rs4986764	*BRIP1*	0.86	0.72	1.04	0.113	0.583	1.10	0.59	2.06	0.753	0.956
rs4987876	*ATM*	1.02	0.76	1.36	0.896	0.992	0.28	0.09	0.90	**0.020**	0.520
rs569143	*MRE11A*	0.84	0.70	1.01	0.059	0.473	0.82	0.46	1.46	0.507	0.840
rs5744934	*POLE*	1.15	0.91	1.45	0.249	0.642	0.98	0.43	2.25	0.969	1
rs601341	*MRE11A*	0.87	0.72	1.05	0.147	0.624	1.01	0.58	1.73	0.989	1
rs6413436	*RAD52*	1.22	1.01	1.48	**0.036**	0.473	0.65	0.36	1.15	0.136	0.736
rs664143	*ATM*	0.83	0.69	1.01	0.055	0.473	1.39	0.77	2.49	0.266	0.757
rs7182283	*NEIL1*	0.96	0.80	1.16	0.690	0.936	0.56	0.31	1.01	0.068	0.709
rs735943	*EXO1*	0.93	0.78	1.12	0.455	0.878	1.48	0.79	2.77	0.211	0.757
rs7797466	*PMS2*	1.07	0.85	1.36	0.560	0.936	2	0.71	5.63	0.512	0.840
rs799917	*BRCA1*	1.01	0.83	1.22	0.934	0.992	1.32	0.70	2.47	0.388	0.819
rs8305	*POLI*	1.25	1.02	1.53	**0.032**	0.473	0.60	0.31	1.15	0.123	0.709
rs861528	*XRCC3*	1.20	0.96	1.49	0.112	0.583	1.05	0.54	2.03	0.881	1
rs861531	*XRCC3*	1.01	0.83	1.22	0.937	0.992	0.95	0.52	1.74	0.872	1
rs861539	*XRCC3*	0.95	0.79	1.15	0.622	0.936	0.86	0.47	1.56	0.619	0.913
rs9350	*EXO1*	0.99	0.78	1.28	0.992	0.992	0.32	0.14	0.78	**0.014**	0.520
rs963248	*XRCC4*	1.02	0.80	1.30	0.887	0.992	0.95	0.44	2.03	0.886	1
rs9876116	*MLH1*	1.02	0.85	1.22	0.843	0.992	1.17	0.63	2.18	0.624	0.913
rs9894946	*TP53*	0.77	0.56	1.04	0.092	0.546	0.83	0.61	1.13	0.229	0.757

GC, gastric cancer; OR, odds ratio; CI, confidence interval.

[a]ORs adjusted by gender, age, *Helicobacter pylori* infection, and smoking status.

[b]QFDR-values obtained after applying the False Discovery Rate (FDR) test.

P-values <0.05 are highlighted in bold.

Supplementary Table 11: Haplotypes in DNA repair genes and association with GC risk.

Gene	SNPs	Haplotype	Frequency HC	Frequency GC	OR (95% CI)*	*P* value
APEX1	rs1130409	GC	0.3739	0.3529	Reference	
	rs1760944	TA	0.2579	0.2638	1.08 (0.87 - 1.33)	0.4743
		TC	0.2505	0.2703	1.14 (0.90 - 1.45)	0.2746
		GA	0.1177	0.1129	1.02 (0.72 - 1.43)	0.9212
ATM	rs1801516	GGC	0.3864	0.4109	Reference	
	rs4987876	GGT	0.3838	0.3544	0.86 (0.71 - 1.03)	0.0940
	rs664143	AGC	0.1364	0.1505	1.04 (0.81 - 1.33)	0.7626
		GTC	0.0934	0.0842	0.85 (0.64 - 1.13)	0.2665
BRCA1	rs1060915	TAC	0.6500	0.6359	Reference	
	rs1799966	CGT	0.3258	0.3447	1.08 (0.91 - 1.29)	0.3657
	rs799917					
BRCA2	rs144848	TAA	0.4131	0.4150	Reference	
	rs1799955	GAA	0.2768	0.2953	1.06 (0.87-1.29)	0.5805
	rs1801406	TGG	0.2241	0.2202	0.97 (0.78-1.20)	0.7520
		TAG	0.0846	0.0686	0.80 (0.58-1.11)	0.1778
ERCC1	rs3212948	CCG	0.6040	0.6079	Reference	
	rs3212961	GCT	0.2514	0.2499	0.99 (0.82 - 1.19)	0.9191
	rs3212986	GAG	0.0940	0.1006	1.08 (0.82 - 1.42)	0.6033
ERCC2	rs13181	TAGT	0.4639	0.4506	Reference	
	rs1618536	GGAG	0.2649	0.2698	1.04 (0.86 - 1.26)	0.6610
	rs1799793	TGGG	0.1573	0.1369	0.91 (0.72 - 1.15)	0.4394
	rs238406					
ERCC3	rs4150416	TGT	0.3970	0.4147	Reference	
	rs4150441	TAT	0.2784	0.2959	1.02 (0.84 - 1.25)	0.8399
	rs4150474	GAG	0.2587	0.2322	0.86 (0.70 - 1.05)	0.1417
		GAT	0.0658	0.0572	0.83 (0.58 - 1.18)	0.2973
ERCC6	rs3793784	CA	0.5372	0.5623	Reference	
	rs4253160	GT	0.4258	0.4049	0.91 (0.77 - 1.07)	0.2543
EXO1	rs1047840	GGCC	0.2735	0.2780	Reference	
	rs1776148	GATC	0.1460	0.1418	0.92 (0.69 - 1.24)	0.5839
	rs735943	AATC	0.1454	0.1416	0.93 (0.70 - 1.24)	0.6165
	rs9350	AGTC	0.0952	0.0749	0.79 (0.55 - 1.14)	0.2077
		GGTC	0.0671	0.0873	1.18 (0.79 - 1.76)	0.4165
		AGCT	0.0722	0.0660	0.90 (0.62 - 1.30)	0.5658
		GGCT	0.0585	0.0550	0.95 (0.63 - 1.45)	0.8211
LIG4	rs1805386	TC	0.6982	0.6891	Reference	
	rs1805388	CC	0.1692	0.1649	0.98 (0.79 - 1.23)	0.8816
		TT	0.1326	0.1459	1.12 (0.87 - 1.42)	0.3780
MLH1	rs1540354	TGGTGG	0.3350	0.3281	Reference	
	rs1799977	TAACAA	0.2410	0.2429	1.03 (0.83 - 1.28)	0.7602
	rs1800734	TAGCAA	0.1476	0.1505	1.05 (0.82 - 1.34)	0.7130

	rs2286940	TAGTGG	0.1396	0.1403	1.03 (0.80 - 1.33)	0.8309
	rs4234259	AAGCAA	0.1215	0.1085	0.93 (0.71 - 1.21)	0.5832
	rs9876116					
MRE11A	rs569143	CG	0.4895	0.5232	Reference	
	rs601341	GA	0.4438	0.4108	0.86 (0.73 - 1.02)	0.0873
		GG	0.06520	0.06490	0.95 (0.68 - 1.32)	0.7410
MSH2	rs1981928	TT	0.7227	0.7276	Reference	
	rs2303428	AT	0.1810	0.1627	0.90 (0.72 - 1.12)	0.3330
		AC	0.0943	0.1096	1.14 (0.87 - 1.49)	0.3343
MSH3	rs10079641	CCAG	0.3845	0.4021	Reference	
	rs1650697	CCGG	0.1773	0.1823	0.98 (0.76 - 1.25)	0.8473
	rs26279	CTGA	0.1341	0.1330	0.94 (0.73 - 1.22)	0.6430
	rs26779	CTAA	0.1134	0.0907	0.76 (0.55 - 1.05)	0.1004
		GCAA	0.0975	0.0903	0.89 (0.66 - 1.20)	0.4304
		CCAA	0.0603	0.0560	0.87 (0.59 - 1.28)	0.4744
MSH6	rs1800935	TATT	0.4574	0.4839	Reference	
	rs2020911	CTTG	0.1597	0.1954	1.15 (0.92 - 1.43)	0.2267
	rs2348244	TTCT	0.1356	0.1132	0.79 (0.61 - 1.03)	0.0762
	rs3136228	CATG	0.1132	0.1046	0.89 (0.66 - 1.18)	0.4166
		TATG	0.0701	0.0606	0.84 (0.60 - 1.18)	0.3051
OGG1	rs1052133	CT	0.6140	0.6230	Reference	
	rs293794	GT	0.2137	0.2023	0.93 (0.76 - 1.15)	0.5062
		CC	0.1687	0.1705	0.99 (0.79 - 1.25)	0.9558
PMS2	rs2228006	GAG	0.4481	0.4521	Reference	
	rs2345060	GGG	0.2496	0.2227	0.89 (0.72 - 1.09)	0.2671
	rs7797466	AAG	0.1508	0.1623	1.06 (0.83 - 1.35)	0.6342
		GAA	0.1475	0.1629	1.09 (0.86 - 1.38)	0.4831
RAD52	rs11226	CT	0.5969	0.5477	Reference	
	rs6413436	TC	0.3225	0.3533	1.19 (1.00 - 1.41)	0.0494
		TT	0.0778	0.0959	1.34 (0.99 - 1.81)	0.0594
WRN	rs1346044	TT	0.6382	0.6738	Reference	
	rs1800389	CC	0.1345	0.1232	0.87 (0.68 - 1.12)	0.2796
		TC	0.1331	0.1204	0.87 (0.67 - 1.12)	0.2713
		CT	0.0942	0.0826	0.83 (0.61 - 1.14)	0.2533
XPC	rs2228000	CC	0.3958	0.3923	Reference	
	rs2228001	TA	0.3275	0.2844	0.87 (0.72 - 1.06)	0.1658
		CA	0.2767	0.323	1.18 (0.97 - 1.45)	0.0965
XRCC1	rs25487	GC	0.3756	0.3842	Reference	
	rs3213245	AT	0.3655	0.3442	0.88 (0.74 - 1.06)	0.1685
		GT	0.2406	0.2526	1.00 (0.81 - 1.24)	0.9756
XRCC2	rs2040639	AG	0.4649	0.4347	Reference	
	rs3218536	GG	0.4363	0.4616	1.13 (0.95 - 1.33)	0.1605
		GA	0.0988	0.1036	1.13 (0.85 - 1.50)	0.4128
XRCC3	rs1799794	GAGGC	0.2575	0.2444	Reference	
	rs1799796	AAATT	0.2273	0.2469	1.15 (0.91 - 1.45)	0.2452

	rs861528	AGGGC	0.2428	0.2237	0.96 (0.76 - 1.21)	0.7108
	rs861531	AAGTT	0.1466	0.1320	0.94 (0.72 - 1.24)	0.6761
	rs861539	AAGGC	0.1173	0.1316	1.16 (0.88 - 1.52)	0.2948
XRCC4	rs13180316	GTTA	0.3073	0.31894	Reference	
	rs1478485	ACGA	0.2521	0.22915	0.90 (0.72 - 1.12)	0.3596
	rs2075685	GCGA	0.1730	0.1677	0.95 (0.73 - 1.23)	0.7048
	rs963248	GCGG	0.1111	0.12020	1.00 (0.75 - 1.34)	0.9823
XRCC5	rs1051677	TAGT	0.4413	0.4477	Reference	
	rs1051685	TAGC	0.3271	0.3142	0.94 (0.78 - 1.14)	0.5551
	rs207906	CAGC	0.0882	0.0970	1.09 (0.81 - 1.46)	0.5885
	rs2440	TGAC	0.0797	0.0771	0.95 (0.70 - 1.30)	0.7626

GC, gastric cancer; OR, odds ratio; CI, confidence interval.
Haplotypes with frequencies > 0.05 are shown in the table.
Odds ratios and 95% confidence intervals were calculated taking as a reference the more common haplotype.

Supplementary Table 12: Characteristics of candidate SNPs analyzed in the study.

SNP[a]	Pathway[b]	Gene	Chr	Position[c]	SNP Type	Alleles[d]	MAF	HWE[e]	Total N (%)
rs3219489	MMR	*MUTYH*	1	45331833	Q324H	G/C	0.27	0.542	1192 (98.8)
rs3219484	MMR	*MUTYH*	1	45334484	V22M	G/A	NA	NA	—
rs1048771	HR	*RAD54L*	1	46278228	A730A	C/T	0.12	0.412	1126 (93.4)
rs1136410	BER	*PARP1*	1	226367601	V762A	T/C	0.13	0.263	1206 (100)
rs735943	MMR	*EXO1*	1	241866849	H354R	C/T	0.47	0.086	1201 (99.6)
rs1047840	MMR	*EXO1*	1	241878999	E589K	G/A	0.39	0.932	1190 (98.7)
rs1776148	MMR	*EXO1*	1	241879243	E670G	G/A	0.39	0.863	1200 (99.5)
rs9350	MMR	*EXO1*	1	241885372	P757L	C/T	0.15	0.215	1195 (99.1)
rs1863332	MMR	*MSH2*	2	47402759	Upstream	A/C	0.08	0.032	1027 (85.2)
rs2303426	MMR	*MSH2*	2	47403411	Intronic	G/C	NA	NA	—
rs1981928	MMR	*MSH2*	2	47445336	Intronic	T/A	0.27	1.000	1200 (99.5)
rs2303428	MMR	*MSH2*	2	47476361	Intronic	T/C	0.10	0.153	1204 (99.8)
rs3136228	MMR	*MSH6*	2	47782677	Upstream	T/G	0.35	0.717	1197 (99.3)
rs2348244	MMR	*MSH6*	2	47792346	Intronic	T/C	0.13	1.000	1205 (99.9)
rs1800935	MMR	*MSH6*	2	47795976	D180D	T/C	0.29	0.682	1197 (99.3)
rs2020911	MMR	*MSH6*	2	47803699	Intronic	A/T	0.35	0.533	1204 (99.8)
rs4150474	NER	*ERCC3*	2	127275751	Intronic	T/G	0.24	0.199	1203 (99.8)
rs4150441	NER	*ERCC3*	2	127283339	Intronic	A/G	0.41	0.733	1199 (99.4)
rs4150416	NER	*ERCC3*	2	127288972	Intronic	T/G	0.31	0.457	1204 (99.8)
rs207906	NHEJ	*XRCC5*	2	216148178	T524T	G/A	0.12	0.351	1205 (99.9)
rs1051677	NHEJ	*XRCC5*	2	216205525	3′ UTR	T/C	0.09	1.000	1204 (99.8)
rs1051685	NHEJ	*XRCC5*	2	216205653	3′ UTR	A/G	0.10	0.062	1204 (99.8)
rs2440	NHEJ	*XRCC5*	2	216206043	3′ UTR	C/T	0.45	0.804	1203 (99.8)
rs1052133	BER	*OGG1*	3	9757089	S326C	C/G	0.21	0.632	1206 (100)
rs293794	BER	*OGG1*	3	9761943	Intronic	T/C	0.17	0.670	1198 (99.3)
rs2228001	NER	*XPC*	3	14145949	K939Q	A/C	0.39	0.865	1128 (93.5)
rs2228000	NER	*XPC*	3	14158387	A499V	C/T	0.31	0.403	1198 (99.3)
rs1800734	MMR	*MLH1*	3	36993455	5′ UTR	G/A	0.24	0.267	1195 (99.1)
rs1540354	MMR	*MLH1*	3	37002998	Intronic	T/A	0.12	0.124	1202 (99.7)
rs4234259	MMR	*MLH1*	3	37007142	Intronic	A/G	0.49	0.101	1197 (99.3)
rs1799977	MMR	*MLH1*	3	37012077	I219V	A/G	0.33	0.360	1206 (100)
rs2286940	MMR	*MLH1*	3	37028615	Intronic	C/T	0.49	0.120	1200 (99.5)
rs9876116	MMR	*MLH1*	3	37042249	Intronic	A/G	0.48	0.087	1201 (99.6)
rs1802904	CCC	*ATR*	3	142449489	Q2625Q	A/G	0.13	0.264	1202 (99.7)
rs2227928	CCC	*ATR*	3	142562770	M211T	C/T	NA	NA	—
rs1650697	MMR	*MSH3*	5	80654962	V79T	C/T	0.25	0.458	1116 (92.5)
rs26779	MMR	*MSH3*	5	80763384	Intronic	G/A	0.39	0.398	1201 (99.6)
rs10079641	MMR	*MSH3*	5	80798145	Intronic	C/G	0.10	0.381	1182 (98.0)
rs184967	MMR	*MSH3*	5	80854162	Q949R	G/A	NA	NA	—
rs26279	MMR	*MSH3*	5	80873118	A1045T	A/G	0.32	0.110	1203 (99.8)
rs2075685	NHEJ	*XRCC4*	5	83076846	Upstream	G/T	0.44	1.000	1204 (99.8)
rs1478485	NHEJ	*XRCC4*	5	83084708	Intronic	C/T	0.41	0.865	1203 (99.8)
rs13180316	NHEJ	*XRCC4*	5	83163634	Intronic	G/A	0.27	1.000	1194 (99.0)
rs963248	NHEJ	*XRCC4*	5	83238075	Intronic	A/G	0.16	1.000	1205 (99.9)
rs2252775	NHEJ	*RAD50*	5	132582752	Intronic	A/C	0.21	0.062	1202 (99.7)
rs2228006	MMR	*PMS2*	7	5987144	K541E	G/A	0.16	0.053	1126 (93.4)
rs2345060	MMR	*PMS2*	7	5999498	Intronic	A/G	0.24	1.000	1203 (99.8)

rs7797466	MMR	*PMS2*	7	6007152	Intronic	G/A	0.16	0.056	1203 (99.8)
rs3218536	HR	*XRCC2*	7	152648922	R188H	G/A	0.10	0.253	1205 (99.9)
rs2040639	HR	*XRCC2*	7	152678103	Upstream	G/A	0.45	0.566	1194 (99.0)
rs1800389	NHEJ	*WRN*	8	31067041	C171C	T/C	0.26	0.214	1199 (99.4)
rs1346044	NHEJ	*WRN*	8	31167138	C1367R	T/C	0.22	0.563	1199 (99.4)
rs12678588	BER	*POLB*	8	42355555	Q137R	G	0.00	NA	1206 (100)
rs2272615	BER	*POLB*	8	42361530	Downstream	A/G	0.12	0.449	1190 (98.7)
rs1805794	NHEJ	*NBS1*	8	89978251	E185Q	C/G	0.30	0.138	1204 (99.8)
rs1800975	NER	*XPA*	9	97697296	5′ UTR	G/A	0.31	0.637	1197 (99.3)
rs2228526	NER	*ERCC6*	10	49470671	M1097V	A/G	NA	NA	—
rs4253160	NER	*ERCC6*	10	49485920	Intronic	A/T	0.45	0.461	1201 (99.6)
rs2228524	NER	*ERCC6*	10	49532830	L45L	G/C	0.26	0.437	1066 (88.4)
rs3793784	NER	*ERCC6*	10	49539493	5′ UTR	C/G	0.42	0.319	1199 (99.4)
rs12917	DR	*MGMT*	10	129708019	L84F	C/T	0.14	0.865	1065 (88.3)
rs2308321	DR	*MGMT*	10	129766800	I174V	A/G	0.09	0.014	1144 (94.9)
rs2434470	DR	*ALKBH3*	11	43919052	E228D	C/G	0.23	0.911	1198 (99.3)
rs174538	BER	*FEN1*	11	61792609	Upstream	G/A	0.30	0.558	1112 (92.2)
rs601341	HR	*MRE11A*	11	94434611	Intronic	G/A	0.43	0.408	1198 (99.3)
rs569143	HR	*MRE11A*	11	94455221	Intronic	C/G	0.49	0.807	1199 (99.4)
rs4987876	CCC	*ATM*	11	108221910	Intronic	G/T	0.09	0.085	1201 (99.6)
rs1801516	CCC	*ATM*	11	108304735	D1853N	G/A	0.14	0.602	1204 (99.8)
rs664143	CCC	*ATM*	11	108354934	Intronic	C/T	0.37	0.932	1204 (99.8)
rs11226	HR	*RAD52*	12	912647	3′ UTR	C/T	0.43	0.864	1118 (92.7)
rs6413436	HR	*RAD52*	12	913513	Intronic	T/C	0.34	0.926	1203 (99.8)
rs1059262	DR	*ALKBH2*	12	109087930	3′ UTR	T/G	0.18	0.789	1203 (99.8)
rs5744934	NER	*POLE*	12	132643940	S1396N	A/G	0.17	1.000	1200 (99.5)
rs5744751	NER	*POLE*	12	132677409	A252V	C/T	NA	NA	—
rs144848	HR	*BRCA2*	13	32332592	N372H	T/G	0.29	0.154	1201 (99.6)
rs1801406	HR	*BRCA2*	13	32337751	K1132K	A/G	0.30	0.634	1202 (99.7)
rs1799955	HR	*BRCA2*	13	32355095	S2414S	A/G	0.22	0.484	1205 (99.9)
rs1047768	NER	*ERCC5*	13	102852167	H46H	C/T	0.42	0.452	1204 (99.8)
rs17655	NER	*ERCC5*	13	102875652	D1104H	C/G	0.26	0.540	1201 (99.6)
rs1805386	NHEJ	*LIG4*	13	108209565	D568D	T/C	0.17	0.662	1200 (99.5)
rs1805388	NHEJ	*LIG4*	13	108211243	T9I	C/T	0.14	1.000	1113 (92.3)
rs1760944	BER	*APEX1*	14	20454990	Upstream	C/A	0.38	0.364	1090 (90.4)
rs1130409	BER	*APEX1*	14	20456995	D148E	T/G	0.48	1.000	1201 (99.6)
rs10483813	HR	*RAD51B*	14	68564567	Intronic	T/A	NA	NA	—
rs175080	MMR	*MLH3*	14	75047125	L844P	G/A	0.44	0.280	1194 (99.0)
rs861539	HR	*XRCC3*	14	103699416	T241M	C/T	0.37	0.603	1206 (100)
rs1799796	HR	*XRCC3*	14	103699590	Intronic	A/G	0.23	0.375	1202 (99.7)
rs861531	HR	*XRCC3*	14	103706470	Intronic	G/T	0.39	0.794	1192 (98.8)
rs1799794	HR	*XRCC3*	14	103712930	5′ UTR	A/G	0.25	0.669	1201 (99.6)
rs861528	HR	*XRCC3*	14	103716661	Intronic	G/A	0.25	0.727	1116 (92.5)
rs7182283	BER	*NEIL1*	15	75351418	Intronic	G/T	0.47	0.163	1191 (98.8)
rs176641	BER	*POLG*	15	89346951	Upstream	A/C	0.36	0.589	1205 (99.9)
rs3136038	NER	*ERCC4*	16	13919522	Upstream	C/T	0.36	0.262	1202 (99.7)
rs2238463	NER	*ERCC4*	16	13924045	Intronic	C/G	0.38	0.269	1203 (99.8)
rs1800067	NER	*ERCC4*	16	13935176	R415Q	G/A	0.12	0.698	1189 (98.6)
rs1799801	NER	*ERCC4*	16	13948101	S835S	T/C	0.30	0.925	1202 (99.7)
rs9894946	CCC	*TP53*	17	7667762	Intronic	G/A	0.15	0.771	1188 (98.5)

rs1614984	CCC	*TP53*	17	7668134	Downstream	C/T	0.40	0.727	1113 (92.3)
rs1042522	CCC	*TP53*	17	7676154	P72R	G/C	0.25	0.41	1204 (99.8)
rs2074522	BER	*LIG3*	17	35002629	Intronic	G/A	0.08	0.565	1203 (99.8)
rs1799966	HR	*BRCA1*	17	43071077	S1613G	A/G	0.34	0.784	1198 (99.3)
rs3737559	HR	*BRCA1*	17	43082287	Intronic	G/A	0.07	1.000	988 (81.9)
rs1060915	HR	*BRCA1*	17	43082453	S1436S	T/C	0.34	0.781	1203 (99.8)
rs799917	HR	*BRCA1*	17	43092919	P871L	C/T	0.36	0.529	1200 (99.5)
rs4986764	HR	*BRIP1*	17	61685986	S919P	C/T	0.38	0.107	1199 (99.4)
rs4968451	HR	*BRIP1*	17	61849946	Intronic	A/C	0.17	0.778	1201 (99.6)
rs2048718	HR	*BRIP1*	17	61863458	Upstream	C/T	0.42	1.000	1159 (96.1)
rs3730668	BER	*POLI*	18	54269477	Upstream	G/T	0.42	0.080	1192 (98.8)
rs8305	BER	*POLI*	18	54294435	A731T	A/G	0.27	0.672	1206 (100)
rs25487	BER	*XRCC1*	19	43551574	Q399R	G/A	0.37	0.147	1206 (100)
rs25489	BER	*XRCC1*	19	43552260	R280H	G/A	NA	NA	—
rs3213245	BER	*XRCC1*	19	43575535	5´ UTR	T/C	0.39	0.795	1203 (99.8)
rs13181	NER	*ERCC2*	19	45351661	K751Q	T/G	0.34	0.200	1205 (99.9)
rs1799793	NER	*ERCC2*	19	45364001	D312N	G/A	0.32	0.445	1205 (99.9)
rs238406	NER	*ERCC2*	19	45365051	R156R	G/T	0.50	0.121	1206 (100)
rs1618536	NER	*ERCC2*	19	45368348	Intronic	G/A	0.48	0.031	1105 (91.6)
rs3212986	NER	*ERCC1*	19	45409478	Q504K	G/T	0.26	0.524	1126 (93.4)
rs3212961	NER	*ERCC1*	19	45419065	Intronic	C/A	0.12	0.550	1205 (99.9)
rs11615	NER	*ERCC1*	19	45420395	N118N	T/C	NA	NA	—
rs3212948	NER	*ERCC1*	19	45421104	Intron 3	C/G	0.37	0.136	1197 (99.3)
rs20580	BER	*LIG1*	19	48151296	A170A	C/A	0.49	0.287	1200 (99.5)
rs3626	BER	*PCNA*	20	5115125	3´ UTR	G/C	0.13	0.593	1205 (99.9)
rs132788	NHEJ	*XRCC6*	22	41663764	G593G	G/T	NA	NA	—

Chr, chromosome; MAF, minor allele frequency; N, number of individuals successfully genotyped.
NA, not applied.

[a]SNP identification according to the NCBI data base.

[b]DNA repair pathway. BER: base excision repair; NER: nucleotide excision repair; MMR: mismatch repair; HR: repair of DNA double-strand breaks by homologous recombination; NHEJ: repair of DNA double-strand breaks by non homologous end joining; DR: direct repair; CCC: cell cycle checkpoint signalling pathway.

[c]Chromosome position according to the Genome Reference Consortium Human Build 38.p2 (GRCh38.p2).

[d]Major/minor alleles.

[e]Hardy–Weinberg equilibrium *P* values in control population.